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THE GROWTH OF BONE

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THE GROWTH OF BONE

OBSERVATIONS ON OSTEOGENESIS

AN EXPERIMENTAL INQUIRY INTO THE DEVELOPMENT AND REPRODUCTION OF DIAPHYSEAL BONE

BY

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PREFACE.

THIS inquiry was undertaken to test by direct experiment problems connected with the growth of bone. It was necessary, as a firm belief exists that all periosteum produces bone,—such is the physiological teaching,—many believing that diaphyseal bone could not be produced without periosteum, and once produced would die were the periosteum removed. Some of the experiments most vital to the maintenance of this belief are here shown to be fallacious. Prior experience in human physiology had indicated that the periosteum was not osteogenic, but not so convincingly to the mind of others, as direct experiments have demonstrated. The evolution of the osteoblast, the exhibition of its independent vitality and proliferating power both within the diaphysis and without in the midst of the soft tissues have been here demonstrated. The great reproductive power of growing bones inherent in the diaphyseal extremities at their epiphyseal cartilages is shown in striking manner in many of the experiments. Without a full knowledge of this power the filling up of blanks in the shafts of growing bone might readily be attributed to the periosteum instead of to its true cause, the osteogenic potency of the growing shaft.

The experiments were conducted for the most part on the canine species of three varieties all in the developmental period.

Had the experiments here related been arranged chronologically the earlier ones would have been those which formed the basis of papers presented to the Royal Society, one of which is published in the *Philosophical Transactions*, Series B, Vol. 199, pp. 253-279; and they also constituted the fundamental part of the Banks Address on Surgery delivered in the University of Liverpool. The remainder of the direct experiments and observations appears now for the first time.

The author has gratefully to acknowledge the assistance of Mr. J. A. C. Macewen in the experimental work and in the revision of proofs: and the aid in carrying out the experiments received from Dr. Mort, late University Assistant, and Dr. Shaw, Research Scholar in the Surgical Department of the University. His indebtedness is also due to Sister Douglas for some of the illustrations, and to both her and Sister Saunders for help in photography.

GLASGOW,
December, 1911.

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CHAPTER I.

THE GENESIS OF THE OSTEOBLAST.

In the study of the evolution of the osteoblast, one sees in the foetal shaft that diaphyseal ossification proceeds through cartilage. The nuclei of the cartilage cells divide and are set free as osteoblasts and synchronously the cartilage envelope disappears. Diaphyseal cartilage seems but a phase in bone formation. In adult life regeneration takes place either through a transition stage of cartilage or by direct division of bone cells into osteoblasts. Where the conditions are most favourable, the osteoblasts are formed directly from the bone cell and ossification is hastened; but when the conditions are less favourable, the cartilage cell is formed and ossification is retarded. When cartilage does exist, the nucleus of the cartilage cell under certain conditions seems to possess the power of rapid proliferation and frees itself from its envelope by what looks like a process of absorption of the envelope without the intervention of osteoclasts,—except under special circumstances,—and also apparently without leucocytic phagocytosis. The nuclei thus set free are of the same form and size as the neighbouring osteoblasts; they proliferate like them, play the same rôle and cannot be distinguished from them. The osteoblast is the embryonic

or 'free form' of the bone cell, and once formed is capable of great and rapid proliferation; it has also the power of producing a matrix which becomes calcified.

In repair of bone, a transitional cartilaginous stage is general, which is prolonged if untoward conditions prevail, but under favourable circumstances the osteoblasts develop directly into bone without passing through transitional cartilage. In fractures freshly made and at once accurately coapted, there is not only a minimum of transitional cartilage but a direct proliferation of osteoblasts and a rapid transformation of these into mature bone. Such is seen frequently after osteotomies followed by immediate coaptation of the fragments.

THE EPIPHYSEAL CARTILAGE.

The existence of cartilage at the epiphyseal plates is evidence of the continued growth of bone at that part. Freedom from undue pressure, one of the conditions necessary for active osteoblastic proliferation, is obtained at the epiphyseal lines, where the osteoblasts have room to grow and where they receive abundant pabulum to stimulate their increase, their growth at this part being regulated and ordered by the ossifying cartilage, while the limiting membrane—the periosteum—keeps it within the confines of the shaft. If similar conditions obtained in other parts of the diaphysis, osteoblastic proliferation would ensue toward the part where pressure resistance was least. If an hiatus in the shaft occurred, osteoblastic proliferation would tend to fill it up, and if the periosteum were removed over the surface of a gap in the shaft the uncontrolled proliferation might be so great as not only to fill the gap but to form a node or callus-like mass on the outside. The growth occurring at the normal epiphysis is governed by inherent heredity, that

taking place to fill a gap is not so governed and may be irregular in form, dependent on the local conditions.

When the cartilage at the epiphysis disappears, solidification follows, after which epiphyseal proliferation is retarded or arrested. The physical conditions apropos of increased osseous proliferation at the epiphyseal lines and at other parts of the diaphysis then become equal. Before the occurrence of synostosis at the epiphyseal lines, the increase in linear extension would likewise cease if external pressure prevented its expansion. When such pressure is exerted, the inherent, proliferating power of the diaphyseal osteoblasts being checked, it occasionally shows itself in other directions, such as in increased diaphyseal thickening from interstitial growth, or lengthening of the bone in the opposite direction to that of the fixed diaphysis, interfering with the alignment of the articular surfaces or in bending of the shaft.

Though growth in a linear direction normally occurs from increments made to the extremities of shafts toward their epiphyses, this obtains because of the congenial conditions pertaining thereto. Were such conditions arising in other parts of the diaphysis, increase in osteoblastic proliferation would follow at such parts. Were a portion of the entire circumference of the growing shaft removed, growth of bone would form centripetally from either extremity of the sectioned diaphysis, to fill this gap. In such a case, increments may also be made at the epiphyseal cartilage, which, instead of adding to the length of the bone, might travel in the direction of least resistance, which in this instance would be toward the gap in the middle of the shaft.

Were the epiphyseal plates of cartilage removed, the osteoblasts from the pre-existing ossified diaphysis, being relieved from confinement, would pour out from

the freshly sectioned shaft into and through the gap, and fresh bone formation would ensue and continue to augment until solidification caused soldering of the freshly formed bone to the shaft and the epiphysis. Small diaphyseal grafts, when placed in a gap in the continuity of bone, show active proliferation from the whole circumference, each piece being an ossifying centre from which osseous tissue is thrown out sufficient to fill the gap between the various fragments and to unite them together along with the two ends of the divided shaft. Under suitable surroundings the vegetative capacity of the osteoblasts is at least as great as any of the tissues in the body, and bone proliferation takes place from its whole surface circumferentially, while epithelium for instance proliferates only on the flat.

Evidence of interstitial growth of bone.—It is said that bone can only grow in length and breadth by the superposition of fresh osseous increments to its periphery, therefore that linear increase must be due to diaphyseal deposits at the epiphyseal lines, and circumferential increase by depositions under the periosteum. In these two situations the conditions suitable for bone expansion prevail. The soft, elastic epiphyseal cartilage at the extremities, and the layer of loose areolar tissue under the periosteum afford relief from undue pressure, room to expand and proliferate, and also supply abundant pabulum from thin-walled vessels.

Bone is living, and as every living tissue requires renewal, absorption and repair must be constantly recurring processes throughout life.

These can only be carried out by interstitial changes. It is true that in the depths of well-formed diaphyseal tissues, great and rapid interstitial changes are retarded owing to the mechanical resistance offered by the hard

osseous walls. When stimuli are applied to bone, the cells in the interior proliferate and escape into the Haversian canals and are carried peripherally into the first space suitable for their expansion, which is generally the sub-periosteal areolar tissue. There they have room for further proliferation and may ultimately contribute to the breadth of the shaft. Such changes occur within a few days. While this is taking place, however, absorption of the calcareous tissue in the interior has begun, and areas of softening are formed. The conditions suitable for expansion prevail, space is provided for the proliferation of the osteoblasts which form interstitial growth in the interior of the shaft and may expand the bone peripherally.

These facts may be illustrated by physical action. A pin driven into the diaphysis, so that it is firmly caught, will, in the course of a few days, become loose, owing to the softening which the mechanical stimulation has set up in its periphery. The greater the pressure, the greater the area of softening. When the pin is withdrawn, the aperture which is left in the bone is rapidly filled by interstitial proliferation. If a wire be made to surround bone, and firm traction be made upon it—to maintain two pieces of bone in apposition, for instance,—absorption goes on in front of the wire and continues until the strain on the wire is overcome—until it reaches a position of rest. There it will remain embedded in the osseous tissue generated in its wake by fresh, interstitial growth.

The continued pressure of a soft india-rubber drainage tube placed between or on bones produces at the part pressed on localised absorption of the bones, so that a hole is made in the bones, corresponding to the circumference of the tube, and often osteoblasts, relieved from

their limiting membrane, escape and form an ossified mould round the tube. The effect of the soft tissues in maintaining the form of the bone may be considerable, even the weight of the tissues have their result. The tongue, physically at least, is a soft organ, and yet its complete removal often produces in the course of years a marked alteration in the shape of the lower jaw, which generally falls inwards so as to permit the teeth to slope markedly toward the buccal cavity. Normally the form of the lower jaw is maintained by the soft tissues within the mouth.

Bone absorbs under pressure more easily than cartilage, as may be seen in the vertebrae under aneurismal pressure.

The inherent interstitial capacity for reproduction of bone is manifest in grafts from the interior of the diaphysis, which proliferate freely whenever placed in suitable conditions.

Great interstitial changes occur in bones during and after constitutional disturbances. In rickets the calcareous matter is absorbed during the period of ramollissement, afterwards it is re-deposited, in some cases to excess, and a period of eburnation occurs. Shafts may be altered in shape, not merely by bending, but by remodelling. A shaft which was normally broadest antero-posteriorly may become broadest in the opposite diameter, which could not occur without fresh interstitial changes. Those changes may take place with great rapidity. Within a couple of weeks of a severe illness, the bones of children have softened so as to be bendable, thus they participate in the systemic weakness which may be evinced by flabbiness of the muscles and general debility. During ensuing convalescence these same bones have become in a few weeks hard, active interstitial

changes having taken place during both periods. Within a month or six weeks the calcareous matter in some instances has been absorbed, eliminated from the system, and a fresh supply has been ingested and re-deposited.

Interstitial changes in syphilitic osseous lesions are abundant, even in the interior of the shafts, rarefaction and re-deposition occurring often, accompanied by increased thickening and weight in the bones. In certain forms of anaemia absorption and thinning of the bones occur; and in others, which are at least accompanied by anaemia, the thickness and weight of the bone are greatly increased. The influence of certain chemical agencies and the effect of the secretions of certain glands of the body (pituitary, for instance), seem to have an influence on interstitial growth of bone. The influence which trophic nerves exert on osseous tissues is manifest in the alterations ensuing in the long bones as the result of tubercle of joints, and in the epiphysis in locomotor ataxia.

The solidity and hardness which diaphyseal bone presents are apt to convey the impression of immutability, whereas there are few animal tissues more prone to interstitial change, or more responsive to varying systemic conditions. Though the bone cell in its mature state is surrounded by calcareous walls, it is not imprisoned thereby, each cell controlling its immediate area. The inherent power of the bone cell calls forth the calcareous depositions within the area of its influence, and retains the power of dispersing it. When the bone cell dies, the calcareous fabric that encircled it remains inherently immutable, and then requires external agencies for its removal, such as phagocytes within or mechanical interference from without.

THE PERIOSTEUM.

The periosteum has been described as a fibrous membrane, composed of two layers, the inner of which "contains many elastic fibres and blood vessels in a minute state of sub-division." Besides these two recognised layers, however, there is a quantity of loose areolar tissue existing between the inner of the two layers of the periosteum and the bone. This subperiosteal areolar tissue is admirably adapted for cell growth. It is sufficiently loose to permit of easy penetration by the osteoblasts emanating from the underlying osseous tissue, and it has in its immediate vicinity, especially during developmental periods, abundant pabulum from thin-walled vessels from which these cells may be nurtured and proliferation encouraged.

In adult life the periosteum is closely adherent to the shaft of the long bones. In children and adolescents, while it is firmly attached to the extremities of the diaphyses at the junction of the epiphyseal plates of cartilage, yet all over the shafts of the long bones between these two plates the periosteum is loosely adherent, and may be easily shelled from the bone. So loosely is it attached that in many instances a potential space may be described as existing between the inner layer of the periosteum and the bone. This potential space and its contained areolar tissue may be the sphere of physiological and pathological processes. Osteoblasts which, owing to increased stimuli, have generated in too great numbers in the osseous tissue, may be extruded from the Haversian canals. The induction of pyogenesis in the medullary canal is followed by an enormous osteoblastic proliferation in the osseous tissue of the shaft, which is rapidly extruded on to the surface of

the bone, filling the areolar meshes, where the osteoblasts ultimately form osseous plaques firmly adherent to the periosteum. So rapid is the osteoblastic reproduction that, within a few hours of the thermic indication of the medullary infection, proliferation of osteoblasts has already occurred.

When the pyogenic process has invaded the subperiosteal areolar tissue, it spreads with great rapidity, converting the potential space into a pus-filled cavity with bare bone on one side and the periosteum on the other, while at either extremity it is limited by the epiphyseal plates.

The periosteum aids in the nutrition of the bone on account of the abundance of blood vessels and lymphatics which it contains and which are distributed to the bone through the Haversian canals. Yet the shafts of long bones are chiefly nourished through the nutrient vessels, and, as long as they remain intact, the bone can live and have its peripheral circulation restored, even after the destruction of the periosteum.

In healthy, adult life, the subperiosteal areolar tissue contains few or no osteoblasts, and, if this tissue be detached from its overlying bone, no osteoblastic reproduction can ensue from such periosteum. The fact that when bone grows subperiosteally, osteoblasts are found in the subperiosteal areolar tissue, and that they are absent from that tissue when no ossification takes place there, causes one to connect the regeneration of bone occurring under such circumstances with the presence of osteoblasts, and raises the question as to whether the periosteum has the power of generating osteoblasts or whether their presence there is merely incidental to underlying tissue changes in the shaft itself. The latter view is probable, from the fact that, after the bone is

deprived of its periosteum, such interstitial osseous changes are followed equally by osteoblastic proliferation on the surface of the nude bone and into the meshes of the connective tissue covering the muscles.

The subperiosteal areolar tissue surrounding the shafts of mature, healthy bone contains few or no osteoblasts; but if certain stimuli be applied to the osseous tissue of such shafts, osteoblasts are increased in the Haversian canals and are found to accumulate in the subperiosteal areolar tissue at first round the blood vessels issuing from the Haversian canals, and afterwards generally through the areolar tissue surrounding the area of irritated bone. Notwithstanding softening of the bone, due to such changes, the proliferated bone cells cannot find sufficient room at first in the bony substance or within the hard-walled Haversian canals, but they are accommodated in the subperiosteal areolar tissue, where they are freed from the unyielding walls and supplied with abundant pabulum from thin-walled vessels.

After the developmental period has passed, if from mature, healthy bone, the periosteum be detached and transplanted, no ossific production results; but if, before detaching the periosteum, the underlying osseous tissue be subjected to stimuli, and if the subperiosteal areolar tissue be thereby filled with osteoblasts, osseous production after transplantation may ensue to an extent limited by the osteoblastic supply.

THE BEHAVIOUR OF THE OSTEOBLASTS AND THE PRODUCTION OF BONE IN ACUTE OSTEOMYELITIS.

In acute osteomyelitis the infection is at first located in the medulla. In consequence of the great hyperaemia induced beyond the area of infection, stimulating rapid tissue change and hyperplasia, the bone cells which are

beyond the area of pyogenic invasion are converted into their embryonic condition and proliferate with great rapidity. Osteoblasts accumulate in the Haversian canals, and, owing, *inter alia*, to the centrifugal blood pressure, are extruded on to the surface of the shaft, where they infiltrate the meshes of the loose areolar vascular tissue which exists between the periosteum and the bone. The meshes of this layer become charged with osteoblasts, from which fresh layers of bone ultimately form. If the pyogenic invasion be progressive, the shaft may be involved and die; but prior to this necrosis, the osteoblasts which have escaped into the periosteum are preserved from destruction. If in a case of osteomyelitis the periosteum be removed from the bone at a very early stage, osteoblasts will still be poured out on to the surface of the shaft, and form there a layer of fresh bone between the muscles and the old bone. This has been directly observed on several occasions.

If the central pyogenic infection be early detected and removed within a few hours of its first manifestation, then not only will the infective process be arrested and the sequent osseous destruction prevented, but, the irritation being removed, the bone tissue will proliferate only to a slight extent, and the subperiosteal areolar tissue will receive very few osteoblasts, and little or no peripheral thickening of the bone will ensue.

Delay in removal of the infective product from the medulla, besides increasing the destruction of the parts, permits great osteoblastic proliferation and subsequent osseous development, which is mainly peripheral, but which is also interstitial, and may be even central in these parts of bone which are beyond the sphere of pyogenic infection.

This is the usual course in osteomyelitis, but it does

not always follow in this way. Occasionally necrosis of the whole shaft occurs without reproduction of bone under the periosteum. This may arise from one of at least two causes. The first occurs when the pyogenic invasion is more virulent, rapid and extensive, causing blockage of the vessels not only of the medulla, but also of the shaft, producing necrosis without a preliminary period of hyperaemia, and consequently before regenerative tissue changes have had time to occur in the shaft. The second, where the main nutrient vessels of the shaft at a very early stage become thrombosed by pyogenic invasion, the blood supply of a large portion of bone is cut off and necrosis occurs before proliferation within the bone can take place. In some such cases the periosteum participates in the destructive process, but it does not do so in all. Owing to its separate blood supply, it is possible for the periosteum to live, and it sometimes does so apart from the bone. In such a case, however, there is no regeneration of osseous tissue, there having been no osteoblasts regenerated from the bone and thrown from the shaft into the subperiosteal areolar tissue before necrosis set in.

THE PERIOSTEUM AS A LIMITING MEMBRANE TO THE OSTEOBLASTS.

The periosteum acts as a limiting membrane to the osteoblasts issuing from the interior of the bone. This is well illustrated in fractures. When a fracture takes place without rupture of the periosteum, the union of bone occurs so perfectly that it is difficult after a time to discover the seat of fracture, and at no time is there much if any provisional callus. This obtains likewise in fractures occurring in lower animals when the periosteum remains intact.

When the periosteum and bone are simply incised, as in osteotomy, and the cut osseous tissues are at once accurately coapted and kept at perfect rest, ossification ensues with little or no callus, and in a short time it is difficult to detect the seat of the lesion.

If, on the other hand, the fracture has been attended by tearing of the periosteum, and the limb has been subjected to much movement, subsequent to the production of the osseous lesion, then the osteoblasts are poured out from the fractured surfaces into the gap between the bones, from which they are extruded into the surrounding soft tissues. The limiting periosteal membrane having been ruptured, the free movements to which the limb is subjected will express the osteoblasts and blood accumulated in the osseous gap, and these osteoblasts will form fresh osseous deposits outside the bone.

Again, in malposition of the fragments, the ossific matter is often poured out in great abundance; but if there be on any side a continuity of the periosteum, it will limit the osseous deposit at that part. Frequently, in fractures, the ossific material poured out from the bone lesion covers the periosteum. In such a case the overlying callus is only loosely attached to the outside of the periosteum covering the bone, and may be easily peeled off unless the periosteum becomes absorbed, when intimate organic adhesion between bone and callus takes place.

The potency of the periosteum as a limiting membrane is seen when, in cases of fracture, it is torn up and stretched across the fractured surface of one of the fragments. It here forms an effective barrier against osseous union, the ossific formation being absolutely limited by the periosteum, and fibrous union results.

In compound fractures many opportunities have been afforded of demonstrating how frequently the periosteum

is torn from one fragment and laid over one or other of the fractured surfaces, where, had it been allowed to remain, non-union would have occurred.

On several occasions, during operation for un-united fracture, the interposition of the periosteum between the fragments has been found by me to have been the sole cause of non-osseous union. Were it not for the fact that the periosteum is normally so tightly stretched over the bone, delayed and non-union would be more frequently met with after fractures due to the interposition of the periosteum between the fragments.

Reference may be made to Experiment U, where a new deposition of bone causing an increased thickening of the growing shaft occurred over an area from which the periosteum (the limiting membrane) had been removed, an osseous ridge or node having thus been formed.

THE EPIPHYSES.

The epiphyses are made up of cancellous tissue enclosed for the most part in synovial membrane, either within the sac or covered by a duplicature of the membrane. The articular surfaces of the epiphyses are clothed with cartilage, and there is a potential space between the articular cartilage and the hard layer of bone covering the cancellous osseous tissue. This is especially seen in children and adolescents. Into this potential space blood is sometimes extravasated—imparting a blue colour to the overlying cartilage. In diseased processes emanating from the epiphyses, this potential space is frequently filled with pathological products before the cartilage is shed.

Once the epiphyseal plates of cartilage are well formed and complete, they become of service against the advance of pathological products—as they then form

a barrier to disease emanating from either the epiphysis or the diaphysis. In this way a pyogenic process emanating from the medulla of the diaphysis is prevented from spreading into the epiphysis, and consequently the joint is saved from invasion; and on the other hand a tubercular process originating in the epiphysis is barred from encroaching on the diaphysis. In infancy and early childhood, before the epiphyseal plates have been well formed, and while there are still blanks in the cartilaginous formation of those plates, the barrier to pathological invasion is imperfect, and consequently pyogenic processes may spread from the diaphysis into the epiphysis and into the joint. Tubercle may in like manner spread from the epiphysis through the imperfectly formed epiphyseal plate.

The same differences are manifest between the two in the selective localisation of disease. Tubercle is a common disease in the epiphysis, while it seldom involves the shaft *de novo.* Osteomyelitis invades the diaphyses and seldom implicates the epiphyses except by extension.

The process of repair in the diaphyses, including the growing cartilage, differs from that in the epiphyses. The ossific formation produced in the repair of diaphyseal bone is much more abundant than that produced in the repair of the epiphyses. This may be seen in fractures where the callus from the shaft is abundant, when the periosteum has been ruptured or removed so as to allow the osteoblasts to escape, while in the epiphysis, which has no periosteum—and does not require such—the repair is accompanied by a minimum of ossific formation. This difference in the amount of callus produced in the diaphyseal and epiphyseal bone is due to properties inherent in the two forms of osseous tissue, and not to the presence or absence of the periosteum. The fact

that there is no periosteum over epiphyseal bone is in accordance with the fact that there is a very modified tendency to the production of callus in epiphyseal osseous tissue; consequently it requires less a limiting membrane to control the osteoblasts from forming an exuberance of growth, as such does not occur therein. If, after injury, callus formed to the same extent in the epiphysis as in the diaphysis, the movements of joints would be much more seriously interfered with after fractures through the epiphyses than they are.

This difference is *one* of the factors in explaining how, during the developmental period, certain fractures at or near joints, such as the elbow, are much more prone to produce anchylosis from callus formation than others. Those that produce anchylosis from large masses of callus are chiefly situated on the diaphyseal side of the bone, passing through the epiphyseal cartilage—such as T-shaped fractures—while those that do not, are confined to the epiphyses on the articular side of the cartilaginous plate which is left intact.

It is interesting to remember, in this relation, the difference between the reproduction of bone from the epiphysis and that from the diaphysis. If, in the case of excision of the elbow joint, the excision be within the epiphyseal lines, then the reproduction of bone is strictly limited; but if in the growing humerus the diaphysis has been encroached on, the osteoblasts from the refreshed surface of the diaphysis are apt to be disseminated, so as to produce thickenings attached to the ends of the bone and even to infiltrate the surrounding soft tissues and consequently produce impairment of movement. This is especially seen in the case of excision after fractures of the shaft of the humerus involving the epiphyseal line.

CHAPTER II.

HAS THE PERIOSTEUM INHERENT OSTEOGENIC POWER?

For the purpose of testing the osteogenic reproductive power of the periosteum, the following experiments were performed:

Experiment K. Preservation of Periosteum and Removal of a Portion of the Diaphysis subperiosteally.—Shaft of radius removed subperiosteally to the extent of $1\frac{3}{4}$ inches, the periosteum being carefully preserved and being left *in situ.*

There was no attempt made to detach plaques of bone which might have adhered to the periosteum during its separation. At the upper extremity of the shaft an irregular spike-like process of bone was left. The wound was then closed, the soft tissues being allowed to coalesce. A case of plaster of Paris was applied loosely to the limb to prevent pressure from without.

No bleeding.—Aseptic wound healing resulted, leaving no visible cicatrix and no adherent scar. After removal of plaster four weeks subsequently, there was no apparent union, a gap being detected between the extremities of the radius. At the end of six weeks, the gap was quite marked and the ulna was still bending.

Examination of Specimen 10 Weeks After.—The

right ulna had markedly bent, and this bending had lessened greatly the interval which would otherwise have existed between the two extremities of the un-united radius. At the part from which the bone had been removed and the periosteum had been left intact, there was a gap, void of osseous formation, but filled with dense connective tissue.

When this was turned aside, the proximal portion of the bone was seen to be flattened laterally, a new formation of bone continuous with the shaft projecting toward the gap (Fig. 1).

A somewhat similar formation had taken place below. So that, with the exception of the flattened, osseous, new bone produced from the growth of the shaft, there was a complete gap between the ends of the bone at the part where the bone had been removed and where the periosteum was left intact. The periosteum therefore did not reproduce bone—otherwise the gap would have been filled.

Comment.—In this case, as is usual in the young, the new growth from both epiphyseal lines was rapid, and would have been sufficient to have filled a gap of less dimensions. So rapid is the growth from the epiphyseal lines in the young that, in experiments planned to test the respective reproductive value of the periosteum and the bone itself, the results might be disconcerting to those not fully cognisant of the degree of the power and celerity of diaphyseal growth from the epiphyseal plates. Credit for osteogenesis might thus erroneously be attributed to the periosteum. In order to eliminate this element, and the possibility of error therefrom, it was resolved to remove subperiosteally the whole bone—epiphyses as well as the diaphyses. Were bone reproduced under these circumstances from the periosteum which remained, the periosteum would have all the

FIG. 1.—PRESERVATION OF PERIOSTEUM AND REMOVAL OF PORTION OF SHAFT OF BONE.

The specimen shows result 10 weeks after.—The portion of the shaft which was removed subperiosteally is seen between the two large specimens. The figure on the right is the radius and ulna of the normal limb for comparison.

credit. With this object experiment W was undertaken.

Experiment W. To Test the Power of the Periosteum to Produce Bone.—The whole shaft of the radius was removed subperiosteally, including both epiphyses, both proximal and distal joints having been opened. The periosteal tube, from which the bone was removed, was left *in situ* with all its attachments to the soft tissues intact.

In course of disarticulating the head of the radius from the ulnar articulating surface, the periosteum of that part of the ulna had been slightly detached, and the bone was scraped by the periosteal elevator.

The radius was preserved as removed for future comparison. Aseptic healing resulted. Examination at the end of three weeks showed that no new bone had formed. The animal did not use the paw much at this period.

Specimen Examined Six Weeks After.

Radius.—There was no reproduction of radius. An entire blank existed where the shaft had been. Traces of a fibrous cord marked the position of the periosteum which had been left.

Ulna.—From the radial articular surface of the ulna, a somewhat ovoid, scale-like osseous flake sprang. Its greatest length was three-quarters of an inch and its greatest breadth was three-eighths, while its thickness was about one-eighth of an inch (Fig. 2).

Toward the lower third of the ulnar shaft there was an osseous nodule formed in a tendinous structure attached to the bone. It was half an inch long by one-sixteenth to one-eighth of an inch in thickness.

The styloid portion of the ulna was bent at an angle, and a small spiculum of new bone projected from it (Fig. 3).

Comment.—The result of removing the whole radial shaft, while leaving the periosteum intact and attached to the soft tissues, has been that no new shaft formed; there was an entire absence of ossific reproduction from the periosteum. It is the more striking as this has occurred during the most rapid period of osseous development of the skeleton generally.

NOTE.—In the canine species the head of the radius is closely attached to the ulna—much more intimately so than in man—there being limited rotatory movement in the canine elbow joint. Consequently the head of the radius is more difficult to detach from the ulna, and the latter more apt to be damaged.

In several experiments on epiphyseal growth, where the shaft of the bone has been removed subperiosteally, the periosteum being preserved intact, it is seen that the growth of bone resulting from a damaged epiphysis was attenuated and dwarfed, while that which ensued from the undamaged epiphysis was normal in strength and thickness, the two portions presenting a marked contrast to each other. Had the periosteum which was left intact produced the bone, it would have done so equally throughout the whole length of the extent of the periosteum, and as much toward one epiphyseal extremity as the other. (See Experiment Q.)

CAN A PERIOSTEAL FLAP PRODUCE BONE WHILE LEFT STILL ATTACHED AT ONE END AND ENCIRCLING MUSCLE AT THE OTHER?

Experiment U. To test the Osteogenic Power of the Periosteum when partially detached from the Bone and placed among the Muscles.—A longitudinal portion of periosteum was elevated from the right radius in such a manner as to leave the upper end still attached to

FIG. 2.—SUBPERIOSTEAL REMOVAL OF RADIUS, A TUBE OF PERIOSTEUM BEING LEFT INTACT. THE RADIUS HAS DISAPPEARED, THE ULNA IS LEFT.

Subperiosteal removal of radius including epiphyses. Specimen shows *result* 6 *weeks after*. Total absence of radius. Osseous and fibro cartilaginous growth from damaged radial articular facet on ulna. At lower third tendinous expansion showing toward extremity osseous nodule, size of barley grain.

FIG. 3.—SUBPERIOSTEAL REMOVAL OF RADIUS, RESULT SIX WEEKS AFTER. SHOWING TOTAL ABSENCE OF RADIUS.

Same as No. 2, opposite side, with the radius which was subperiosteally removed at time of operation placed alongside for comparison. The styloid process of the ulna has been bent from pressure and an osseous nodule—about the size of a barley grain—projects from its extremity.

the epiphyseal line and the ligamentous structures at the head of the bone, while the strip was otherwise free (Fig. 4). This flap measured two inches in length and quarter of an inch in breadth. The free end of this strip of periosteum was made to penetrate between the muscular fasciculi of an adjacent muscle and was then brought back to the radial shaft, where its free extremity was stitched to the cut edge of the radial periosteum at the distal side of the part from which the periosteal flap had been raised.

If the periosteum produced bone, a spiral osseous ring encircling the muscular fasciculi would be expected to result.

It was hoped that the attachment of the periosteum to the epiphyseal line and soft structures continuous with the head of the bone, would ensure a blood supply to the periosteal strip, without permitting the extrusion of the osteoblasts from the bone along the detached portion of the periosteum. The blood supply would be further aided by the extremity of the flap being attached to the cut edge of the periosteum covering the bone.

Result.—Eight weeks after the specimen was secured.

Examination.—At the part of the diaphysis from which the periosteum was removed there was now a considerable new deposition of bone causing an increased thickening of the shaft. An osseous node was thus formed on the radius at the part where the limiting membrane (the periosteum) had been removed (Fig. 5). At this point there was a close investment of the bone by the adjacent muscles—causing a muscular adhesion —from infiltration of osteoblasts and connective tissue.

Round the muscular fasciculus, through which the periosteal strip had been drawn, a fibrous tissue band

could be traced, but there was no bone formation at any part surrounding the muscle.

Comment.—Therefore, from the part of the shaft from which the periosteum was removed, there was an increased thickening of bone, and there was no bony formation round the muscle resulting from the encircling periosteal strip.

The limiting membrane being removed over a portion of the radius, the osteoblasts pour out on the surface and form an osseous thickening—a node—and by infiltration of the adjacent muscles they become closely attached to the shaft—thereby restricting the muscular contractions.

Experiment Y.—As Experiment U showed that a flap of periosteum raised from the shaft of the radius, while it remained attached at its proximal epiphyseal line, and which was made to surround the muscle, did not result in bone formation, it was thought advisable to try a fresh experiment with a periosteal flap left this time adherent to the periosteum of the shaft instead of to the soft tissues near the epiphyseal line.

A flap of periosteum was raised from the right radius. It was detached below, and it remained continuous with the periosteum on the shaft above. It measured one inch and a half in length and three-eighths of an inch in breadth. It was placed round one of the muscular fasciculi of an adjacent muscle, its lower border was then fixed to the cut edge of the periosteum remaining on the radius. Union by first intention ensued.

Result.—Seven weeks after the specimen was obtained. A trace of a connective tissue strand encircling the muscle was all that remained of the periosteal flap. There was no bone or any calcareous matter in the line of the scar.

Comment.—One would not have been surprised to find

FIG. 4.—SCHEMA.

Schema showing flap of periosteum raised from bone except at proximal extremity, encircling muscular fasciculus and stitched to border of intact periosteum at lower end.

FIG. 5.—REMOVAL OF FLAP OF PERIOSTEUM FROM RADIUS.

Result 8 *weeks after*.—Showing a node-like increase of bone on shaft of radius at the part from which the periosteum was removed.

osseous reproduction from osteoblasts which had escaped from the bone and which had been raised in the periosteal meshes during the removal of the flap. There was, however, no evidence of osseous growth; thus confirming Experiment U.

CAN HETEROTOPIC, TRANSPLANTED PERIOSTEUM PRODUCE BONE?

A flap of periosteum two and a half inches in length (afterwards shrinking to two and a quarter) was removed from the entire circumference of the bone and was placed in line with and partially surrounding the left jugular vein. The wound healed by first intention.

Seven weeks subsequently this flap had disappeared, except a fibrous nodule the size of a pea containing as a kernel a small osseous nodule. This osseous nodule was found at one extremity of the place where the periosteal flap had been. Doubtless this nodule resulted from a minute osseous plaque, or from some osteoblasts adherent to the periosteum in process of removal. Had it generated from the periosteal flap, the whole length of the flap would have produced bone equally over its two and a quarter inches of surface. (See Experiment X.)

Again, two portions of periosteum were found totally absorbed seven weeks after having been transplanted into the tissues at the back of the neck. There was no bone formation. (See Experiment N.)

In cases where bone is said to have been produced from transplanted periosteum, bone plaques must have been raised from the bone in process of removal of the periosteum, and have been transferred along with it.

Subperiosteal excision of the elbow bears this out. This operation has been performed by me over two hundred times—237. In the performance of the excision great

care must be exercised to prevent osseous growth within the new joint, which, did it occur, would limit or prevent free movement. Consequently, after removal of the diseased parts, the periosteum is carefully scrutinised in order to remove all visible and tangible osseous plaques which may have been adherent to the periosteum, while forcibly detaching it from the bone. The result is that an excellent joint with free movement is uniformly secured without fresh development of bone, except in those cases where the humeral diaphysis has been encroached on, when from the sectioned diaphyseal surface fresh bone may protrude.

If the periosteum were raised, however, with plaques of bone adherent to it, regeneration of bone would ensue from such pre-existing bone. The same would occur if the osteoblasts infiltrated any portion of the areolar tissue surrounding the soft parts. Were one artificially or pathologically stimulating osteogenesis within the bone, the osteoblasts would be forced on to the surface of the shaft and become entangled in the meshes of the subperiosteal areolar tissue. Were the periosteum then removed such osteoblasts would continue to grow and would give rise to the so-called periosteal formation of bone. In such a case, however, the process is the same as if bone were removed from the shaft in bulk—it is the proliferation of the osteoblast which has produced bone in either case—not the periosteum.

In osteomyelitis one sees the same phenomena. Beyond the area of pyogenic invasion, the diaphyseal osteoblasts are regenerated in great number during the early period of inflammation in the medulla, and are extruded from the Haversian canals into the subperiosteal areolar tissue filling the potential space between the bone and the periosteum.

CHAPTER III.

OSTEOGENIC POWER OF BONE BEREFT OF PERIOSTEUM.

THE PERIOSTEUM AS A LIMITING MEMBRANE TO THE OSTEOBLASTS.

The periosteum has been regarded in these pages as a "limiting membrane" to the osteoblasts which may be extruded on to the circumference of the bone. As long as the periosteum remains intact, the osteoblasts are thus prevented from being scattered among the damaged soft tissues, and from entangling the muscular fasciculi, the tendons and their connective tissue investments. When the periosteum is removed from the bone, the osteoblasts which are poured out intermingle with the injured soft parts and do so most effectively, when they have been disseminated by persistent movement, and when the soft parts and the muscular fasciculi have been torn and their interspaces filled with blood clot. These are the conditions best adapted for the dispersal, proliferation, and ultimate maturation of the extruded osteoblasts. When the muscles are preserved intact they resist osteoblastic infiltration, and their fasciculi do not readily become surrounded with osteoblasts. Under these circumstances, however, the muscles and soft parts are readily pushed aside to accommodate the osteoblastic mass which after consolidation, from its presence and

irregular shape, is apt to impair muscular function. During the early period of osteoblastic deposition, while the young osseous mass is being formed, and while it is still plastic, occasional gentle, well regulated, muscular movement aids in moulding the effused osteoblasts into a form more suitable for the maintenance of normal muscular function.

The modifying influence of pressure.—In the same way external pressure may exert a modifying influence upon the size and shape of the young osseous mass while it is still plastic, and may prevent fixation about the joints from callus forming in such positions as would interfere with movement. This is illustrated in fractures about the humeral condyles, especially when the distal position of the diaphysis is involved. If the limb be placed in the straight position, and the anterior surface of the fracture be free from pressure, callus forms in the soft tissues in front of the fracture, and when consolidated becomes a barrier to flexion of the elbow joint. Whereas, if pressure be exerted from the outset on the young plastic bone, by flexion of the elbow upon the humerus, this osseous effusion is less in bulk, and so flattened upon the shaft, as to present little or no impediment to free flexion of the elbow joint.

The cells in the normal growing bone, by their inherent power, control their own increase and development quite apart from the periosteum. The form and size of the growing bone is governed chiefly from within, and only slightly, if at all, by its external covering, which on the other hand is responsive to the osseous demands, elongating and widening as required. Whatever be the periosteal increase necessitated to accommodate the osseous growth, the periosteum always presents an unbroken barrier to the commingling of

FIGS. 6 AND 7.—THE PRODUCTION OF CALLUS IN THE LOWER ANIMALS.

Anterior Aspect.

Posterior Aspect.

Healing of fracture under the periosteum in the red deer.

young osseous tissue from within with the soft parts without.

As long as the physiological action of the periosteum continues, it aids in moulding and retaining within bounds any plastic osseous effusion which may form on the surface of the shaft. In pathological conditions the periosteum may become altered physically. It may be overstretched by the rapid production of pyogenic products accumulating between it and the bone. In some cases of osteomyelitis, the periosteum from having become overstretched has lost its elasticity and form, and permits great and irregular accumulations of superimposed ossific matter to be deposited. Even in such a case, the periosteum still acts as a barrier between the soft tissues and the embryonic bone cells.

In the same way, if the bone be injured as by subperiosteal fracture, the amount of callus poured through the fractured fissures in the bone is controlled by the periosteum, being limited in amount and modified in form by the overlying membrane. So that in subperiosteal fractures there is very little appearance of callus—sometimes the amount is not detectable. From the more accurate position secured, and the prevention of callus attained, the adjacent muscles in such cases remain absolutely unaffected. These subperiosteal fractures heal more quickly, and the functional result is much better than in those fractures in which the periosteum is ruptured and the osteoblasts are allowed to escape to form callus in the soft tissue. The same phenomena appear in the formation of subperiosteal gaps in the shaft made for the relief of osseous deformities. When a linear osteotomy for genu valgum is performed on the inner two-thirds of the femoral condyles (supracondylar method), the outer third of the shaft

is stretched until a wedge-shaped gap is left—covered by periosteum. The wedge-shaped gap fills rapidly with osseous tissue, without overflow, as the limiting membrane prevents that. Hence there is no obtruding callus on the outer femoral aspect to restrict muscular movement. On the inner side, even though the linear periosteal wound is still patent, there is little protruding callus owing to immediate and accurate coaptation of the sectioned bone and its subsequent perfect rest. The mechanical conditions obtaining prevent its outpouring.

In a fractured bone with ruptured periosteum, the amount of callus is apt to be larger when treated simply by splints than when the fracture is exposed, the blood and the outpoured embryonic osseous tissue removed, and accurate coaptation and fixation secured.

The modifying influence of consolidation of bone in arresting further proliferative activity is great. The bone cell has then reached its maturity when it lives its life and performs its function. It is, however, ever ready when required to disperse its calcareous surroundings, and again take on active proliferation in its embryonic form.

IS THE PRODUCTION OF CALLUS INHERENTLY GREATER IN THE LOWER ANIMALS THAN IN MAN?

Fracture in the Lower Animals.—It is believed by many that the lower animals are inherently prone to excessive formation of callus after fracture, and especially does it seem great in them when compared with the amount which is poured out after fracture in man.

Abundant formation of callus is found after fracture in the lower animals; but instead of the large amount being inherent to them, may it not be incidental to the single fact of excessive and prolonged movement allow-

FIG. 8.—EXCESSIVE CALLUS FORMATION IN HUMAN FEMUR.

Callus resulting from fracture of upper third of femur.

ing the dispersal of the osteoblasts through the rupture of the periosteum? In the lower animals the periosteum must generally be torn after fracture, owing to the violent movement ensuing. In the following instance, however, it seemed to have remained intact:

Fracture in a Red Deer's Leg, with Periosteum intact.—A deer sustained a broken leg on attempting to get through a wire fence; the leg was seen afterwards dangling and the animal remained standing for a long time, apparently unfit to move. By and by it was able to feed, and it was allowed to remain on the low ground until it was capable of using freely its damaged leg.

About eighteen months subsequently it was shot on the hill, and the specimen was sent to me. The periosteum had remained intact, and the fracture was so perfectly healed that there was no evidence of external callus, except a small spicule at the back (Figs. 6 and 7).

With all the care bestowed on them, many human bones are not so compactly united after fracture. Here, however, the periosteum—the limiting membrane—had remained intact, and the animal had refrained from subjecting the broken part to much movement.

If a human limb be subjected to excessive and prolonged movement after fracture, with tearing of the periosteum, a great amount of callus is thrown out, quite in the same way as is often seen in the lower animals (Fig. 8).

Result of Free Movement after Fracture in Man.—The result of free and continuous movement after fracture in man is well illustrated in the case of a seaman who was shipwrecked in a storm in the Bristol Channel. He had his femur fractured in its upper third, and as he was unable to jump into the boats or to swim, he was tied to a spar which lay on deck.

He lay there in a helpless condition for 48 hours, his fractured leg being washed to and fro by every sea which broke over the wreck. He was then rescued in a semi-insensible condition, and taken on shore to a hospital, where he lay for many months. A formidable osseous mass grew in the muscles of the thigh, all round the fracture; and owing to its bulk and rapid increase, and also to the fact that the bone remained un-united, the question arose in the minds of the surgeons who were treating him as to whether it was of tumour formation. He was ultimately sent to me (1887). He was then unable to walk, from malposition and non-union of the fragments with great shortening of the limb, and also from the tumour-like mass of callus, which caused a large swelling in the middle and upper thirds of the thigh and interfered with muscular movement.

On operation it was found that the osseous tissue had infiltrated the torn muscular bundles, and it was in such masses, many inches thick, that an extensive quarrying with chisel and mallet was required before the normal shaft was exposed.

The bone was placed in proper position and sutured. Rapid healing occurred with only an inch of shortening. The torn muscles from which the osseous masses had to be detached were in many places so short that they were only brought together by plastic operation.

He was ultimately able to walk with slight halt, and to work for his living.

Here the amount of callus and bone formation in the soft tissues surrounding the fracture was relatively as great as in any specimen seen by me taken from the lower animals.

FIG. 9.—GROWTH OF BONE DEPRIVED OF ITS PERIOSTEUM.

Result 12 weeks after.—Showing that a shaft of bone, deprived for the most part of its periosteum, can continue to grow. Its fellow on the normal side is shown for comparison.

CAN A BONE, DEPRIVED FOR THE MOST PART OF ITS PERIOSTEUM, CONTINUE TO GROW?

Doubtless the deprivation of the periosteal blood supply would limit the peripheral increase of bone, just as the partial cutting off of the nutriment of any other part would deduct from its development. Some believe that a portion of bone deprived of its periosteum must die. This does not necessarily follow, as many clinical facts show and the following experiment proves:

THE PERIOSTEUM REMOVED FROM THE ENTIRE CIRCUMFERENCE OF THE DIAPHYSIS OF THE RIGHT RADIUS, THE BONE REMAINING *IN SITU*.

Experiment A.—The periosteum was removed from the entire shaft of the right radius, leaving only quarter of an inch of periosteum on the diaphyseal side of the epiphyseal lines.

The operation was practically bloodless; aseptic healing ensued without visible scar or adherent cicatrix. Along with this specimen the corresponding left radius is preserved for comparison.

Description of Specimen as seen about 12 *Weeks afterwards.*—The shaft of the bone was found to be entirely covered with a layer of newly-formed connective tissue, closely investing the bone and adhering to it much more firmly than periosteal tissue. This fibrous layer was found more difficult to detach from the bone than normal periosteum. The bone was quite healthy, and had acquired an abundant new blood supply. It had not, however, uniformly increased circumferentially quite to the same extent as its fellow on the left side (Fig. 9), but the difference in circumference did not amount to more than one-thirty-second

of an inch in some parts, while in others the two shafts were nearly alike. In many subsequent experiments in which the periosteum was removed, the shaft had abnormally increased circumferentially, and markedly so after partial removal of the periosteum, so much so that nodes were formed at the denuded parts.

DUHAMEL'S SILVER-RING EXPERIMENT.

Duhamel placed (1739) a silver ring under the periosteum in a living animal, and found, some time after, that the ring had become covered by bone. He inferred from this that the periosteum secreted bone. This experiment is often quoted as a proof of the osteogenic power of the periosteum.

There is no doubt about the fact that when a metallic ring which closely fits the shaft of a growing bone is placed under the periosteum, new bone will in course of time surround the ring. The deduction drawn therefrom, that the periosteum must therefore be the source of the new bone, does not necessarily follow. Irritation of a bone excites proliferation of the bone cells, and the osteoblasts are poured out from the Haversian canals on to the surface of the bone and fill the interstices of the soft tissues surrounding the shaft, such as the loose areolar tissue existing between the bone and the periosteum. In this way layers of new bone emanating from the bone itself are deposited peripherally, and may soon cover a foreign body of limited size surrounding the bone or lying on its surface.

If this be so, would bone, denuded of its periosteum, be capable of throwing out sufficient ossific matter to clothe a metallic ring placed upon its surface?

A priori one might infer that the naked bone, being bereft of its periosteal blood supply, might lose to some

FIG. 10.—SILVER RING EXPERIMENT NO. 1.

Result 12 weeks after.—Specimen shows ring completely covered by bone, a small portion of silver ring being exposed by removal of enveloping bone.

extent its osteoblastic, regenerative power, though the abundant inosculations of the numerous branches of the nutrient vessels in the interior of the bone might suffice to supplement the nutrient defect of the periphery of the shaft.

In order to test this, the following experiments were performed :

NEW SILVER-RING EXPERIMENTS.

Experiment B. A Circle of Periosteum removed from the Entire Circumference of the Shaft of Right Radius and a Silver Ring placed upon the Denuded Bone.— A circle of periosteum, comprising the whole circumference of the right radius, and measuring half an inch in breadth, was raised from about the middle of the shaft.

A flattened silver ring was made to encircle the denuded bone at this part. The operation was bloodless, the wound healed aseptically, without visible scar and without adherent cicatrix. The bones of the left limb are preserved for comparison.

Description of the Specimen as seen 12 *Weeks after.* —The right radius was covered, at the part that had been denuded of the periosteum, with a new-formed connective tissue, which was more firmly attached to the bone than that of the normal periosteum on the shaft above and below this part. After the bone was denuded of this new-formed connective tissue and of the periosteum covering the other portions of the shaft, there was no trace of the silver ring to be seen. The shaft of the bone was smooth all over, and if the silver ring still existed it must have become enveloped in the bone. There was, however, a thickening of the shaft at the part from which the periosteum had been

removed, and it was considered probable that the silver ring lay beneath at this point. The shaft was scraped through in a vertical direction, and after penetrating the bone for about one-eighth of an inch the silver ring was exposed completely buried in firm osseous tissue (Fig. 10).

Three other apertures were scraped through at different parts of the circumference of the shaft so as to expose the silver ring at each.

The thickness of the new bone covering the ring in front was fully one-eighth of an inch, and it was a little less behind. Thus the silver ring placed upon the bone, denuded of periosteum, had in three months become completely enveloped in newly-formed bone, one-eighth of an inch in thickness.

The new bone, at the part which was denuded of periosteum, is denser and thicker than that on the other parts of the shaft which were not operated on.

Comment.—Though the results attained in this experiment pointed in the direction that the bone produced the osseous tissue which surrounded the silver ring, it was not conclusive, since, owing to the small circle of periosteum removed, measuring only half an inch in diameter, it might be said by way of criticism that the periosteum at either side might have grown quickly over the gap and then produced the osseous tissue which covered the silver ring. In order to meet this criticism two other experiments were made.

SECOND NEW SILVER-RING EXPERIMENT.

Experiment P.—Two inches of the diaphysis of the right radius, comprising the whole shaft, with the exception of half an inch from either epiphyseal line, were denuded of periosteum, which was entirely removed

FIG. 11.—SILVER RING EXPERIMENT NO. 2.

Result 7 weeks after.—Both silver rings are invisible, being completely covered with bone.

FIG. 12.—SILVER RING EXPERIMENT NO. 2.

Skiagraph showing the two silver rings enclosed in bone. The new bone is very slightly marked in photo, as is usual with X-rays.

along with the superficial osseous layer of the shaft. Two silver rings were then placed upon the centre of the shaft about half an inch apart. During the necessary manipulation, the connective tissue covering of one of the adjacent muscles was encroached on so as to expose the muscular bundles, and these naked muscular fasciculi came into direct contact with the denuded diaphysis.

Aseptic wound healing without visible cutaneous scar resulted.

Description of Specimen as seen 7 Weeks after (6 weeks and 6 days after).—There was no skin scar visible to the unaided eye. The periosteum at the epiphyseal ends was normal and could be separated from the underlying bone readily. Toward the centre of the shaft, over the whole extent previously denuded of periosteum, the soft parts were closely adherent to the bone. In part of the circumference of the shaft, the longitudinal muscular bundles were adherent to the shaft, and the connective tissue surrounding them was also partly infiltrated with osseous matter. At other parts the shaft was covered with dense connective tissue infiltrated with fibro-cartilage and bone nodules, detectable by the unaided sight and also by touch.

Microscopic examination further confirmed this. Had the animal lived a few weeks longer, this tissue would have been converted into well-formed bone.

On exposure of the bone, the shaft was seen to be uniform in outline. The silver rings were nowhere visible, the new bone completely covering them. After thinning the bone at one part, a small portion of one of the silver rings was shown shining through a superimposed layer of bone. The second ring was left buried in the bone without being exposed (Fig. 11).

Comment.—Here were two silver rings placed upon a

denuded shaft bereft of its periosteum, which, seven weeks afterwards, were entirely covered over with newly-formed bone. The newly-deposited bone had in some parts of its circumference a covering of new-formed connective tissue enclosing fibro-cartilage and islands of bone; while in other parts the shaft was covered by adherent muscles infiltrated with osseous matter from the growing bone.

But where the bone was covered by adherent muscle and where it was covered by connective tissue, the silver rings were equally covered over with osseous deposit. Presumably no one will suggest that at the part of the circumference covered by muscle, the muscle deposited the osseous matter covering the ring?

An X-ray photo shows the two silver rings in position covered by new bone (Fig. 12).

THIRD NEW SILVER-RING EXPERIMENT.

Experiment.—A ring of periosteum, measuring an inch in breadth, was removed from the entire circumference of the shaft of the right radius. The superficial osseous tissues were taken away in order to ensure the removal of any remnants of periosteum. In the centre of this denuded shaft, a silver ring was made to encircle the bone so as to adhere closely to the shaft for two-thirds of its circumference, while it bulged beyond the circumference of the shaft for the remaining third.

The gap existing between the bone and the ring, at the part where it bulged, measured from one-thirty-second to one-sixteenth of an inch, the soft tissues being kept apart from the bone at this point to fully that extent, taking the thickness of the silver ring into consideration. There was thus a space left between the

silver ring and the shaft which extended for one-third the circumference of the shaft. Aseptic healing without visible scar ensued.

Examination of Specimen which was obtained over 12 Weeks after (12 weeks and 5 days after).—There was no visible scar. A layer of connective tissue continuous with the periosteum covered the previously denuded shaft of the bone. The silver ring was covered by new bone, and was completely hidden from view for over two-thirds of the circumference. At the part of the ring which had been made to bulge beyond the bone, the surface of the ring was still exposed, though the interval previously existing between the bone and the silver ring had been filled up by new osseous tissue which had also partly covered the thickness of the silver ring (Fig. 13).

The surface of the exposed silver ring was adherent to and closely invested by the connective tissue layer, which was continuous with the periosteum above and below, and yet there was no bone formed between the outside of the ring and the newly-formed connective tissue which adhered to it. This connective tissue layer covering the ring has been left *in situ* in the specimen. There is no osseous growth in this connective tissue, and it is quite smooth and polished where it covers the ring.

Comment.—The osteoblasts emanating from the denuded bone covered the portion of the silver ring which was applied closely to two-thirds of the circumference of the bone, and also filled the gap which existed between the bone and the bulged portion of the ring over the remaining third. Probably, had longer time been given, the osteoblasts emanating from the bone would have covered the remaining portion of the silver

ring. It is to be noted that the connective tissue covering the bulged part of the ring, though closely applied to it, had not produced any ossific material to cover the silver ring. If it did not do so here, is there any evidence to show that it does so at any other part?

Comment on the Results obtained in the Silver-Ring Experiments.—When, in the canine species, the periosteum is entirely removed from the shaft of a long bone, and a silver ring is made to encircle the circumference of the denuded bone, the osteoblasts emanating from the exposed shaft are poured out peripherally, where they become ossified and increase the thickness of the bone, and at the same time cover the silver ring with fresh osseous tissue.

Under suitable conditions the osteoblasts emanating from the bone penetrate the adjacent soft parts. This is seen in the ossific penetration of the newly-formed connective tissue and the exposed muscular bundles which thereby become infiltrated with ossified tissue and adherent to the shaft. At the parts of the circumference where the exposed muscular bundles are placed in contact with the denuded bone, the peripheral increase of new bone to the shaft takes place as uniformly as it does at other parts which have been surrounded by newly-formed connective tissue continuous with the periosteum at the proximal and distal portions of the shaft.

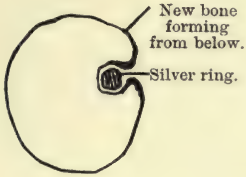
In one of the silver-ring experiments, where a portion of the ring was not covered by osseous tissue, it was observed that the osteoblasts had been poured out from below and had flowed over the sides of the ring, where the mass had become consolidated as if it were lava in process of cooling (Fig. 13A.—Schema).

FIG. 13.—SILVER RING EXPERIMENT
NO. 3

Result 12 weeks after.—Showing gap between bone and silver ring filled with new osseous tissue from the denuded bone.

Had the new osseous growth overlapping the ring emanated from the newly-formed connective tissue growing over the bone in place of the periosteum, the osseous matter would then have been equally distributed over the centre of the ring as well as over the sides.

FIG. 13A.—SCHEMA.



Schema showing newly-formed bone bulging from below and partially overlapping silver ring.

CHAPTER IV.

THE INHERENT REPRODUCTIVE POWER OF BONE MINUS THE PERIOSTEUM.

D AND E BONE GRAFTING—WITHOUT PERIOSTEUM.

Experiment.—Two dogs, D and E, of different species, had the periosteum entirely removed from the right radius, after which a circle of bone, including the whole circumference of the shaft, was removed from each. These circles of bone, about an inch in length, being kept apart, were each divided into small fragments, and those removed from animal D were placed in the gap left in the radius of E, while those from animal E were placed in the gap left in the radius of D.

There was no bleeding. Aseptic healing occurred without visible scar. Osseous union was solid at the end of the fifth week. The left fore-limb is preserved for comparison.

Description of the specimens as seen 12 weeks after transplantation of the bone grafts:

Right Radius of D.—A layer of fibrous tissue covered the whole shaft of the right radius, and was so firmly attached to it that the scalpel, as well as the periosteal elevator, were required to denude the bone. The shaft is entire and continuous in bone formation from one epiphysis to the other, but there is great

FIG. 14.—BONE GRAFTING IN FRAGMENTS MINUS PERIOSTEUM.

Result 12 weeks after.—Continuity of shaft restored, but irregular bone mass resulted, pressing on ulna at seat of grafting.

FIG. 15.—BONE GRAFTING IN FRAGMENTS MINUS PERIOSTEUM.

Result 12 *weeks after.*—Continuity of the shaft restored. Large irregular node formed at seat of bone grafting.

thickening at the part where the graft from the other animal was introduced, and the ulna is consequently pressed on by the osseous mass issuing from the radial grafts (Fig. 14).

In marked contrast to the dense, firmly adherent new formation of connective tissue surrounding the right radius on this limb, was the thin periosteal covering of the left radius (the one which had not been operated on), which shelled with great ease on the application of the periosteal elevator.

Right Radius of E.—There was a dense layer of fibrous tissue covering the bone and firmly adherent to the shaft. The shaft was united throughout, but presented large irregular nodes at the seat of bone grafting. The description of specimen E is very similar to that of specimen D, except that the osseous regeneration in this instance is much greater and more irregular than its fellow D (Fig. 15). It is to be noted in this respect that though the dogs between which the grafts had been interchanged were nearly of a size at the time of grafting, yet one animal was of a variety which ultimately would attain double the size of the other. It is possible that the greater inherent regenerative osteoblastic power in the animal that would ultimately become large, reveals itself in increased proliferation from the grafts, and hence the great increase in the bulk of the graft introduced into E compared with its fellow in D. Though such a possibility might be granted tentatively, other experiments would be required to decide the question.

There are, however, many other determining factors regulating the growth of bone grafts, such as the size of the grafts the amount of blood supply and pabulum

furnished in their new situation, which require to be considered before one can come to a conclusion.

F AND G TRANSPLANTATION OF BONE *EN MASSE*—WITHOUT PERIOSTEUM.

Two dogs, F and G, of different species, had the periosteum entirely removed from the right radius, after which the greater portion of the shaft of the right radius, extending from near the proximal to near the distal epiphysis was removed *en masse* and transplanted, the shaft of the right radius of F being inserted into the gap in the shaft of G, and the shaft of the right radius of G being introduced into the gap in the radius of G.

No vessels required ligation. Aseptic healing, leaving no visible or adherent scar. Firm at the end of four weeks, and subsequent increase in circumference was in F detected through the soft tissues. The left radius and ulna are preserved for comparison.

Description of Specimen F.—The right radius of F seen 11 weeks and one day after transplantation. There was a new formation of dense connective tissue closely adhering to the bone, which was with difficulty elevated therefrom. The shaft, continuous with the epiphyses and firmly united thereto, is greatly increased in circumference, and is much thicker than the radius of the left limb, from which the normal periosteum is easily raised in one piece by the elevator.

Description of Specimen G.—The right radius of G seen 20 weeks and four days afterwards. The newly-formed connective tissue was closely adherent to the transplanted shaft. The diaphysis is united throughout, and so perfect is the union at either end that the insertion can scarcely be made out. It looks like a well-formed normal shaft (Fig. 16).

FIG. 16.—TRANSPLANTATION EN MASSE WITHOUT PERIOSTEUM.

Result 11 *weeks after.*—Showing complete restoration of shaft without undue enlargement.

Comment.—The normal periosteum has a loosely woven areolar tissue existing between the fibrous layer of the periosteum and the shaft. The connective tissue which is formed in place of and after removal of the periosteum is in one rather avascular layer, firmly adherent to the bone. This is seen throughout the experiments, except when the osteoblasts have become attached to the overlying muscles and have fixed these to the bone.

Thus far it has been shown that the bone from the diaphysis can be transplanted in bulk, and that it grows without the intervention of the periosteum. Exception has been taken to this view, as it has been considered possible that the new connective tissue forming over the transplants might have in it some of the elements of the periosteum, and might therefore play the role of the periosteum towards the reproduction of bone. There are several ways of meeting this objection. If the transplanted bone merely played a passive role and the periosteum was the real factor in the reproduction, then the periosteum would produce bone of the same character and appearance whether the transplant were introduced in one piece or in many. Were the reproductive power inherent in the osteoblast, then the smaller the graft, the greater would be the proliferation of the individual cells, as the proliferation would occur from all sides. It has also been alleged that transplants do not live and grow, that they merely play a passive role, and that a new growth does take place into them from either side of the diaphysis. In order to test these theories, the following experiments were performed:

CAN SHAVINGS OF NUDE BONE CONTINUE TO GROW AFTER BEING PLACED BETWEEN THE MUSCLES, AND CAN THEY UNITE TOGETHER AND FORM AGAIN THE CONTINUITY OF THE SHAFT?

Proliferation from bone transplanted in form of shavings.

Experiments N and M.—The shaft of the radius was removed, with the exception of half an inch on the diaphyseal side of the epiphysis. The periosteum was then stripped off from the portion of the shaft taken away.

Two portions of the removed periosteum, about half an inch in length and a quarter of an inch in breadth, were transplanted. One was rolled upon itself and placed under the cellular tissue of the back of the head behind the left ear. The other was placed on the aponeurosis covering the cranium near the right ear. This latter portion was spread out over the aponeurosis.

The shaft of the bone removed, destitute of its periosteum, was then cut into very fine shavings, and these shavings were placed between the muscles, bulging into the gap left in the bone by the removal of the shaft. The neighbouring muscles were then stitched over the bone shavings in order to keep the shavings in position, and especially to prevent them being extruded from the wound.

The wounds healed aseptically without visible scar. The rolled-up portion of periosteum could be palpated under the skin behind the left ear. Three weeks after the operation it was thought to have diminished, and this diminution continued till the end of the fifth week,

FIG. 17.—PROLIFERATIONS FROM BONE TRANSPLANTED IN FORM OF SHAVINGS. (N)

NORMAL BONES.

Shaving experiment No. 1. *Result 7 weeks after.*—Marked increase in circumference of shaft, almost tumour-like in bulk, from proliferation of osseous tissue growing from bone-shavings. The corresponding normal bones are given for comparison.

FIG. 18.—PROLIFERATIONS FROM BONE TRANSPLANTED IN FORM OF SHAVINGS. (N)

Shaving experiment No. 1. *Result 7 weeks after.*—The same in reverse, showing that the increase in osseous bulk has assumed aggressive character, causing pressure and absorption of neighbouring bone.

when the roll of periosteum could no longer be felt externally.

Three weeks after the operation there was apparent union between the bone shavings and the shaft, and a thickening was forming at the part where they had been introduced. This thickening continued to increase in bulk until the end of the seventh week, when the experiment ceased, sufficient time having been allowed to show the result. The animal had grown considerably during the seven weeks.

Examination of the Specimen obtained 7 Weeks after Operation.—There was no naked-eye trace of external wound in the skin. The continuity of the shaft was entirely restored. There was a marked increase in the diameter of the shaft opposite the part where the shavings had been inserted.

The muscles over the new bone had become adherent to it, and at the parts where they were contiguous to the bone their fibres were infiltrated with osseous tissue. So that the longitudinal fibres of the muscle had become embedded in new bone, and these muscular bundles formed the only "periosteum" which the bone had at these places. At other parts of the circumference the new bone was surrounded by newly-formed connective tissue.

When the bone was exposed, the part where the re-implantation of shavings had taken place was represented by a marked circumferential increase in bulk of the shaft —almost tumour-like in proportion—with irregular surface, where the various ends of the shavings, and the proliferated tissue over them, presented externally (Figs. 17 and 18). All the component parts had become fused by osseous tissue into one another and to both ends of the shaft. The actual measurements are :

SHAVINGS, EXPERIMENT No. 1 (N).

Right Radius.

Length of shaft, $4\frac{14}{16}$, nearly 5 inches.

Greatest diameter of nodule antero-posteriorly, $\frac{15}{16}$, almost 1 inch.

Greatest diameter of nodule transversely, $\frac{14}{16}$ of an inch.

Diameter of shaft below expansion ($\frac{1}{2}$ inch) $\frac{8}{16}$ of an inch.

Left Radius.

Length of shaft, $5\frac{2}{16}$ inches.

Greatest diameter in centre of shaft, $\frac{7}{16}$ of an inch (not quite $\frac{1}{2}$ inch). So that the antero-posterior diameter of the nodule was nearly double that of the normal diameter of the shaft and exactly double that of the transverse diameter.

SHAVINGS, EXPERIMENT No. 2 (M).—SHAVINGS AND MARROW, AND WHAT COULD BE EXPRESSED FROM THE BONE.

Result 7 Weeks after.—Right Radius.

Length of shaft, $5\frac{3}{16}$ inches.

Greatest diameter of nodule antero-posteriorly, $1\frac{2}{16}$ inches.

Transversely, $1\frac{4}{16}$ inches.

Left Radius.

Length of shaft, $5\frac{9}{16}$ inches.

Greatest diameter of shaft antero-posteriorly, $\frac{6}{16}$ of an inch.

Transversely, $\frac{9}{16}$ of an inch.

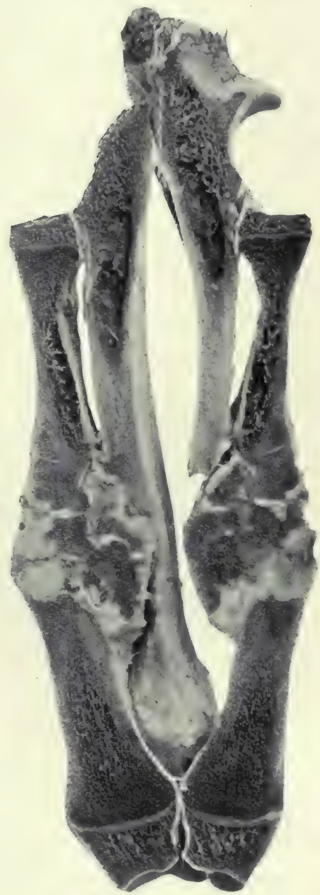
So that the antero-posterior diameter of the nodule was three times greater than the corresponding diameter of the normal shaft, and more than a half greater than the transverse diameter of the normal shaft.

This mass of bone had so far outgrown its normal proportions as to have exercised pressure upon, and caused a marked flattening and indentation of the ulna: just as one sees atrophy and deformity arising

FIG. 19.—PROLIFERATIONS OF BONE TRANSPLANTED IN FORM OF SHAVINGS. (M)

Shaving experiment No. 2. *Result 7 weeks after.*—The specimen in section, posterior view. Contrast the proximal and distal portions of the shaft with the increase in bulk of the grafted shavings.

FIG. 20.—PROLIFERATIONS OF BONE TRANSPLANTED IN FORM OF SHAVINGS. (M)



Shaving experiment No. 2.—Front view of specimen in section, showing ossification proceeding from many centres and all becoming fused together, and to the end of shaft.

in neighbouring bones from pressure effects due to a sarcomatous tumour originating in another bone (Fig. 19).

In making a longitudinal section of the shaft, one sees a number of ossifying centres surrounded by cartilage occurring in the interior of the part where the osseous shavings were inserted, and these are somewhat demarcated by thin layers of cartilage from the growing shaft on either side (Fig. 20).

Comment.—Each of these living osseous particles introduced into the soft parts and between the bones would be quickly bathed with abundance of serous pabulum, which would be sufficient for their immediate wants.

This would be followed by the rapid proliferation of new blood vessels, not only from the surrounding soft parts, but also from the cut ends of the existing shaft, which later would doubtless be followed by osteoblasts which would aid in forming the bulk and in soldering the adjacent bone spicules to the shaft at both ends. The bone cells in the spiculae (shavings), once their vitality was restored, would proliferate and, being set free in the periphery of the fragments, would quickly increase the osseous bulk, each spiculum supplying its quota to filling up the interspace, and collectively to the formation of the tumour-like mass of bone.

How much of the great increase in bulk is to be attributed to the growth from the cut ends of the shaft, and how much is due to the proliferation of the individual osseous shavings, would be impossible to apportion. But each graft as seen in section proliferates from its own centre. The vegetative capacity of the bone cell is as great as that of the epithelial cell, and if one grants not only the viability of the transplanted epithelium, but also its power of extensive proliferation,

then, judging by analogy, the bone cell ought to show, as it has done in this instance, equal capability of living and growing when transplanted. In proportion to the size of the graft, the smaller the graft the greater the proliferation.

If a square inch of living skin were placed upon a raw surface, the regeneration of epithelium would be confined to the margins of the four sides of the square. There would be no proliferation from the interior. Were this square inch divided into 100 square pieces, and these were placed upon a raw surface, each of these pieces would have four sides for proliferation, which would enormously multiply the area of epithelial regeneration.

In the case of this osseous experiment, each graft has thrown out, peripherally, osteoblasts, which have formed round it a new area of bone. Thus every graft has formed a separate centre for ossific proliferation, and in proportion to size, the smaller the graft the greater is the regeneration of bone. The regeneration of bone is proportionately in inverse ratio to the size of the graft.

If two portions of bone of precisely similar size were taken from a shaft, and the one was transplanted whole while the other was divided into small fragments, the former would unite to the shaft at its two sectioned surfaces, and the regeneration of bone would be confined principally to those two surfaces. Therefore, there would be little or no circumferential increase in the line of the shaft. Whereas each of the small fragments into which the latter portion of bone was divided would form a separate centre of ossification, which would throw out osteoblasts from its whole periphery. Consequently, the regeneration of bone in this case would be enormously larger than that which accrues in the undivided transplant and circumferential increase would be assured.

This is what has occurred in the instance here recorded, and other experiments have amply verified the fact.

The ossification emanating from the different grafts can be seen in the section, causing collectively great proliferation, which assumed a tumour-like mass, and produced in its vigorous growth an absorption causing a deep hollow in the neighbouring healthy bone. The new growth from those numerous osseous centres bereft of periosteum has proven itself in the aggregate to be more powerful than the periosteally-covered neighbouring normal bone which was in the same developmental stage.

If the connective tissue, which takes the place of the periosteum after the latter has been removed, and which gradually covers the grafts, showed any osteogenic function, as some believe, then it ought to have produced a uniformity in size of shaft whether the same amount of bone was divided into fragments or was left in one piece. That it does not do so is a fact against the putative osteogenic power of the connective tissue which takes the place of the periosteum, and also against the theory that the remaining diaphysis and not the transplants fill the gap.

HETEROTOPIC TRANSPLANTATION OF BONE.

Two osseous shavings, bereft of periosteum, each about half an inch long and over one-sixteenth of an inch in breadth, were placed into the intermuscular septa on the right side of the neck. In seven weeks they were found to have grown into one dense plaque of bone three-quarters of an inch long and fully quarter of an inch broad by an eighth of an inch in thickness, and the edges of the plaque showed evidence of active osteoplastic growth. (See Expt. X.)

HETEROTOPIC TRANSPLANTATION OF BONE INTO PERITONEAL CAVITY, AND ALSO TESTING THE VALUE OF BONE DUST AS A MEDIUM FOR GRAFTING.

(1) To test whether bone dust from a bur would be of value in reproducing bone when placed between the muscles of the neck.

(2) And also whether slices of bone would live and grow in the peritoneal cavity when fixed to the omentum.

Experiment T.—(1) Bone dust from burring right radius, destitute of periosteum, was placed between the muscles of the neck in contiguity with right carotid artery and between it and the vein.

(2) Several transverse slices of the shaft of the right radius denuded of periosteum were stitched to the omentum in the peritoneal cavity.

(3) A portion of the shaft of the right radius which had been burred into a mere shell, the whole of the soft parts having been burred out, was dropped into the abdominal cavity.

Result 6 Weeks after.—(1) The bone dust from drill which was placed between carotid artery and vein in neck was found absorbed,—all but two minute portions, the size of barley grains, which were seen microscopically to consist of new bone formation.

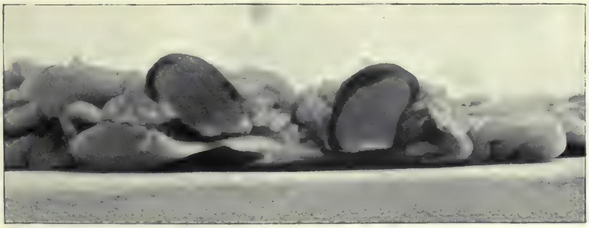
It is possible that the heat evolved by the bur might destroy the osseous cells, and doubtless the minute mechanical trituration of the bone by the bur would help towards destruction of the vitality.

It is probable that a much larger bur with wider teeth (if the heat evolved could be obviated) would have produced pieces of bone of greater consistence and vitality which would have answered the purpose of regeneration

FIG. 21.—HETEROTOPIC GROWTH OF BONE—IN OMENTUM.

Result 6 weeks after.—Shows a rounded mass of bone growing from the flattened slice of the shaft stitched to the omentum. It is covered by a peritoneal layer.

FIG. 22.—HETEROTOPIC GROWTH OF BONE—IN OMENTUM.



The same rounded mass shown in section.

better, but when the whole architecture of the bone is destroyed, the resulting bone dust goes into very small compass, and is unsuited for most practical transplanting purposes.

(2) There was no evidence anywhere of irritation in the abdominal cavity. The transverse slices of the shaft which were stitched to the omentum and placed in the abdominal cavity were now found organically adherent to the omentum, receiving blood supply therefrom. The cut surfaces were rounded over, partly by absorption and partly by slight, fresh osseous deposits.

One of the flattened discs of bone had, however, become enlarged, and a rounded knob projected from its flat surface—a new growth of bone forming inside the peritoneum (Figs. 21 and 22).

All these pieces of bone were beautifully covered by a delicate extension of the peritoneum which formed a translucent capsule over them. There were therefore no adhesions between the bone discs and other organs or peritoneum, with the exception of the omentum, as the foreign bodies were completely invested with a freshly woven garment.

(3) The thin shell of the shaft (left after burring out the soft parts from the diaphysis) was surrounded by a thin veil of extension from the peritoneum, and at other parts by omentum. It had decreased markedly by absorption, but at one extremity—that toward the proximal epiphysis—there was an irregularly formed new growth of bone, quarter of an inch long by one-eighth in breadth.

So that certain portions of this intraperitoneal transplant showed evidence of absorption—and this was the predominating feature—while other portions had increased in bulk by the formation of new growth of bone.

BONE GROWING IN SPONGE.

Is there any direct evidence to show that transplanted living bone actually grows and proliferates instead of forming, like blood clot, a passive framework for the granulation tissue to penetrate, and which framework will then be absorbed?

In this connection an interesting fact was observed, where a minute portion of bone broken off from the deeper layers of a new osseous growth, far removed from any periosteal connection, was found growing in the midst of a sponge filled with granulation tissue.

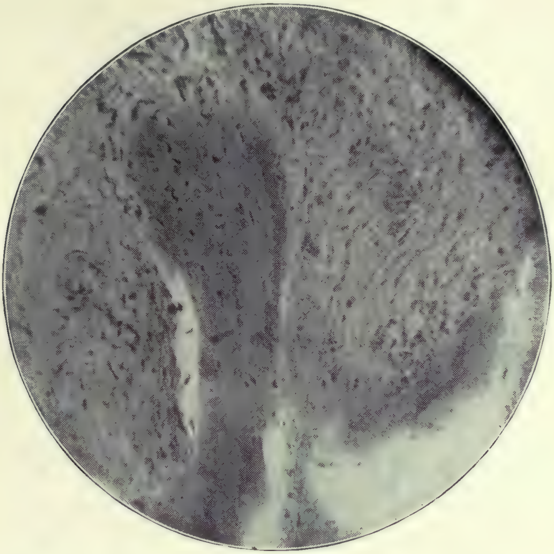
After removal from the fibula of a central sequestrum, measuring 3 inches in length, a hollow cylinder of new osseous tissue was left. Into this hollow cylinder a piece of decalcified, aseptic, specially prepared sponge (Professor Hamilton's method) was being introduced, when it became entangled on an osseous spicule, projecting from the central aspect of the new bone into the lumen of the hollow cylinder.

This spicule became embedded in the sponge so firmly that it was detached from its osseous connections, when the sponge carrying the spicule entangled in its meshes, was introduced fully an inch further into the lumen of the osseous tube and left there.

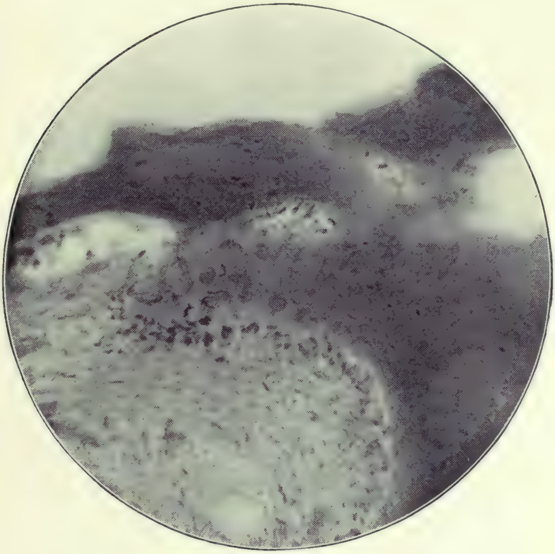
At the end of 11 weeks, when for certain reasons the sponge was removed, it was found filled with granulation tissue, in the midst of which the spicule of bone was seen, and from the extremity of the spicule, which was most deeply buried in the sponge, a knob of what appeared like ossifying cartilage projected.

The sponge and its contents were carefully examined throughout, but there were no other evidences of the presence of bone or ossifying cartilage. The whole

FIGS. 23 AND 24.—BONE GROWN INSIDE OF A DECALCIFIED SPONGE FILLED WITH GRANULATION TISSUE.



Showing new osseous spicule with bone cells and osteoblasts in midst of granulation tissue. ×50.



Showing osteoblasts in process of bone formation. ×150.

spicule was three-sixteenths of an inch in length, and the ossifying knob, which projected from its extremity, was almost one-eighth of an inch in greatest diameter. When this specimen was decalcified and microscopic sections were made, it was seen that the knob consisted of new bone growing from the osseous spicule into the meshes of the sponge framework, and granulation tissue with islets of new bone, which were being increased in bulk by peripheral osteoblastic augmentations. There was no evidence of prior cartilage formation, the ossification seeming to form directly from the osteoblasts. At one part toward the periphery, however, there were traces of cartilage cells in process of devolution, followed at a short distance by bone formation (Figs. 23 and 24).

Toward the base of the spicule, that portion nearest the bone comprising the osseous cylinder, the bone spicule presented lacunar defects filled with leucocytes. The portion of bone nearest the periphery, and, therefore, perhaps, subject to friction, occasioned by the arterial pulsations intensified in a confined space, was undergoing absorption, while its opposite and most central extremity was throwing out ossifying cartilage from the osseous spicule.

This growth of bone took place under adverse circumstances at a distance from immediate contact with other bone, subject to pulsating movements, and in the midst of a sponge filled with granulation tissue.

There was here no possibility of periosteal connection; there was no bone marrow, as the central sequestrum had just been removed and the whole cavity had been thoroughly washed with a free stream of watery solution of carbolic acid, prior to the introduction of the sponge.

The bone formation, though actively occurring in the sponge, was scattered and less purposive than usual, as

if the osteoblasts, while attempting to accommodate themselves to their adverse conditions, had been somewhat confused and indefinite in design.

BONE GROWING IN GLASS TUBE.

Glass-Tube Experiments.—In order to test the osteogenic power of the bone cells constituting the shaft of a long bone, the following experiment was made:

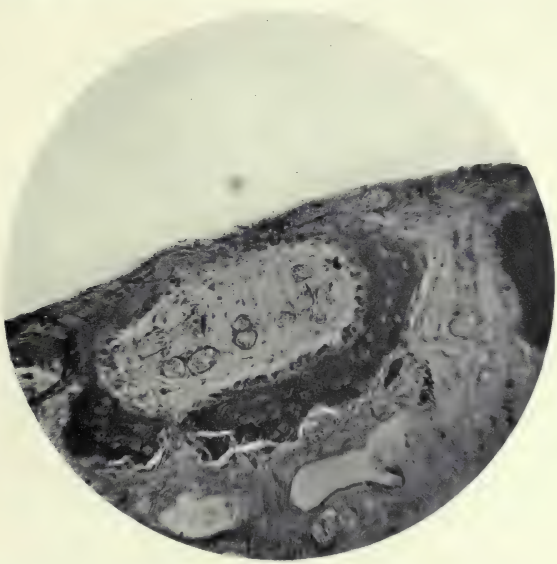
Experiment.—A portion of the entire circumference of the shaft of the canine radius, measuring $1\frac{1}{8}$ inches, was removed, along with its periosteum. Into the gap thus left a glass tube was inserted in such a manner that the distal extremity was firmly fixed into the centre of the osseous tissue of the shaft, while the proximal part abutted against the centre of the shaft above. Some days after, the proximal portion of the tube slipped from its connection with the shaft and lay against the muscles. This relation persisted, though the lower two-thirds of the tube was rapidly surrounded by an osseous mass growing from the shaft which held it firmly in position, while the free end could be felt under the skin with a portion of muscle intervening. The healing was aseptic, without visible scar.

The specimen was examined eight weeks and five days after. The glass tube was found firmly embedded in new-formed osseous tissue, except half an inch which projected beyond the newly-formed bone and abutted on the overlying muscles. Between the projecting portion of the tube and the muscles there was an intervening connective tissue layer which covered the upper portion of the tube and its mouth like a living capsule. Within this capsule, which was translucent, there was a straw-coloured serous fluid which communicated with a drop of fluid within the distal extremity

FIG. 25.—MICROPHOTOGRAPH OF BONE GROWN INSIDE OF GLASS TUBE.

Section taken from the distal part of new growth. Showing peripheral bone formation abutting on the glass tube, while the central portion of the contents consists of blood clot penetrated by granulation tissue containing many thin-walled vessels. ×75.

FIG. 26.—MICROPHOTOGRAPH OF BONE GROWN INSIDE OF GLASS TUBE.



Portion taken from centre of specimen shown in previous illustration. ×150

of the tube. The small quantity of serous fluid in the tube bathed the solid-looking contents within.

On splitting the living capsule, a few drops of serous fluid escaped. The surface of the inside of the capsule —that which was next the glass—was smooth and almost polished. This connective tissue which formed the capsule was continuous with the connective tissue which covered the new bone over the shaft, and yet there was no trace of osseous formation in the capsule. When the capsule was opened, it was found that the glass tube was almost filled with a greyish-red, firm, resisting substance, which, when touched by the probe, conveyed the sensation of a somewhat cartilaginous structure.

The entire lumen of the exposed portion of the tube was filled with this dense material, with the exception of its most distal aspect, where there was sufficient space left to accommodate the drop of serous fluid which occupied it, when the capsule was opened, and which of course communicated with the fluid inside the capsule.

The shaft of the radius was then divided into two in order to expose the relations of the tube to the deeper parts. It was seen that the greater portion of the tube was firmly embedded in the new bone, and that the distal extremity of the glass tube was fixed in the very centre of the diameter of the shaft of the radius at a part where the regeneration of bone was vigorous. The ossific material from the centre of the shaft grew directly into the glass tube and filled it. The material inside the tube could only receive its pabulum and nutriment from the centre of the shaft, as, once inside the tube, the sides of the glass prevented it from coming into contact with the living tissues of

the neighbourhood. Yet, with this constricted area for blood supply, the ossific material grew inside and filled the tube, and thus reached a level beyond the extent of the growth of bone outside of the glass tube.

It is possible that the relief of pressure of the soft tissues aided the ossific material to form more quickly inside of the tube than outside, and the capillarity between the sides of the tube might have facilitated physically the entrance of the osteoblasts.

Microscopic Examination.—A portion of the solid contents were removed from the distal part of the glass tube, the section being made by introducing a narrow-bladed knife within the glass tube, which, after some difficulty, owing to the resistance offered, severed the tissue.

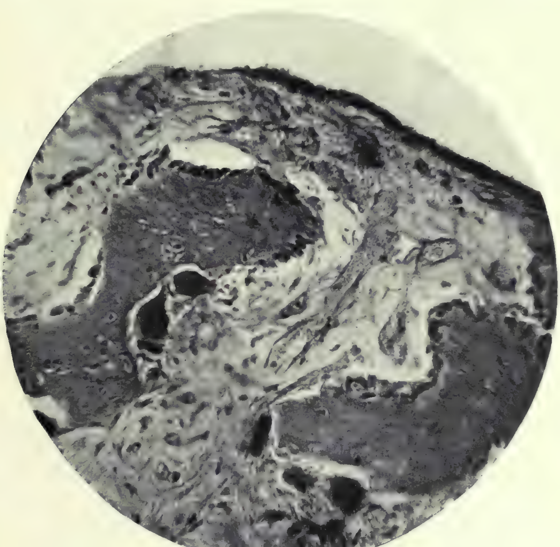
On viewing the cross-section of the portion thus removed, it seemed to consist of an inner and an outer zone of tissue, differing in appearance the one from the other. The inner zone was reddish-grey and somewhat softer than the outer zone. The outer was firm and had a greyish-white colour.

Under the microscope the centre was seen to be made up of highly vascular connective tissue, with here and there traces of osseous formation. The peripheral zone presented a loose areolar reticulum, enclosing many blood capillaries interspersed by numerous islands of bone in process of formation. Most of these bone islands were placed on the external zone of the section, with thin-walled blood vessels of large size on their central aspect and minute blood capillaries on their periphery (Fig. 25). Some of the bone islands, however, abutted on the rim of the glass tube with blood vessels on their central aspect only. In these cases the osseous tissue lay against the lumen of the glass tube with no

FIG. 27.—MICROPHOTOGRAPH OF BONE GROWN INSIDE OF GLASS TUBE.

Showing well formed bone island with osteoblasts in the periphery and in centre, and capillary blood vessels intervening between glass of tube and bone island. ×150.

FIG. 28.—MICROPHOTOGRAPH OF BONE GROWN INSIDE OF GLASS TUBE.



Showing islands of bone and osteoblasts in process of bone formation and several giant cells. ×150.

other tissue intervening. When the sections from the more proximal portion of the tissue in the tube were examined, it was seen that the islands of bone became more numerous and encroached on the centre of the specimen, while the peripheral portions of osseous tissue were better formed than those at the more distal part. The proximal part of the tube was filled with well-matured bone, continuous with the centre of the shaft. This part was left *in situ*, and not submitted to microscopic section.

Comment.—In this instance the bone grew into the glass tube from the osseous tissue in the very centre of the shaft, to the exclusion of all other sources. Neither periosteum nor the surrounding soft tissues could have aided in the production, as access by them to the interior of the tube had not occurred. One sees that the growth of bone enclosed in the glass tube has taken place first in the periphery, and, secondly, centripetally. In this case no increments could be deposited on the outside after the first deposition, as the glass tube limited them in that direction. It was also obvious that the bone cells were deposited abundantly where the capillaries were numerous; and where blood vessels with thick walls alone existed, the osteoblastic development was restricted or absent. One large vessel with thick walls, which formed the nutrient artery of the bone in the glass tube, was not surrounded intimately by bone, though doubtless it supplied the nutriment which flowed through the capillaries for osseous development.

THE EARLIEST APPEARANCE OF BONE GROWTH.

In the second glass tube experiment, the tube first became filled with blood clot, which offered an easily penetrable framework into and through which the

osteoblasts from the centre of the bone could find space to grow, and also in which they could find pabulum from the serous fluid and leucocytal invasion in advance of and following the newly-formed blood vessels.

In the series of microscopic sections, one sees the initial stage of osteoblastic proliferation and the spreading of osteoblasts from common centres through the young embryonic tissue which has penetrated the amorphous blood clot. From these centres the osteoblasts spread peripherally in a somewhat frond-like form, showing the appearance of a midrib, as it were, in the shape of cells surrounding themselves with fixed envelopes fused together in bone-like formation. In the deeper sections the bone formation is more definite, enclosing circular spaces which are gradually being filled with osseous tissue by the proliferating osteoblasts which line them, while the periphery of these osseous plaques are surrounded by multitudes of proliferating osteoblasts. Some of the capillary vessels became surrounded by bone formation, their lumen being gradually narrowed by the ingrowing osteoblasts, so as to resemble Haversian canals, and occasionally the vessels in these spaces become obliterated by the prolific osteoblastic ingrowth.

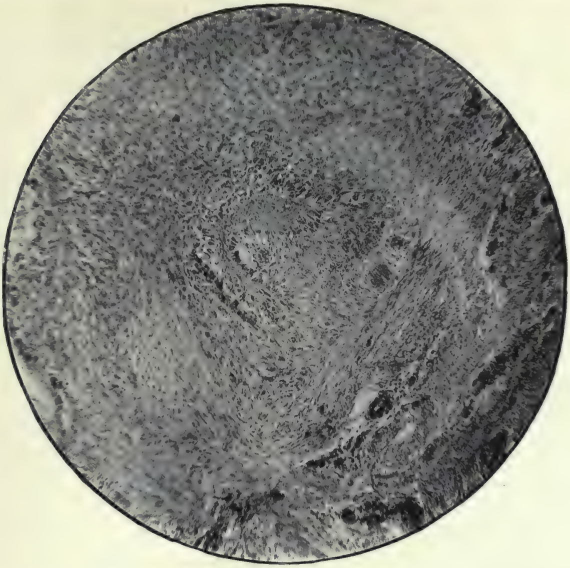
Some parts of the growth inside of the second glass-tube experiment resembled the osseous growth seen in the blood clot forming the wall of a false aneurism, which is shown in this communication.

The growth of bone seemed active where the capillary vessels were thinnest and most primitive in formation. The osseous tissue seemed to grow round these thin capillaries forming a space, in the centre of which the capillary vessel is situated. In these glass-tube experiments there was no trace of a transition stage of

FIG. 29.—MICROPHOTOGRAPH OF BONE GROWN INSIDE OF GLASS TUBE.

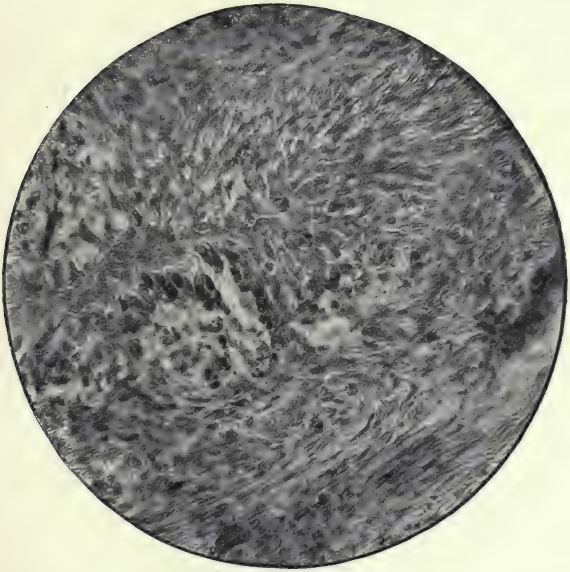
Showing island of bone and osteoblasts on periphery of interior of glass tube—with numerous thin walled vessels. ×66.

FIG. 30.—MICROPHOTOGRAPH OF BONE GROWN INSIDE OF GLASS TUBE—SECOND EXPERIMENT. INITIAL STAGES OF OSTEOBLASTIC BONE FORMATION.



The earliest definite appearance of osteoblastic bone formation within glass tube filled primarily with blood clot. The osteoblastic formation is seen in the centre of the specimen. ×30.

FIG. 31.—INITIAL STAGES OF OSTEOBLASTIC BONE FORMATION—SECOND GLASS TUBE EXPERIMENT.



One of the earliest definite appearances of osteoblastic bone formation. Increased power. ×300.

cartilage cells. Here osteoblasts generated osteoblasts and bone formation became direct.

In considering the results of the experiment of growing bone inside of glass tubes, and noting the readiness with which the osseous tissue penetrates their interior, it was thought desirable to test whether tubes could be made of use in human surgery. By preference a tube ought to be selected sufficiently resistent to maintain the respective distances of the two ends of the shaft from which the piece of the diaphysis was removed, so as to prevent falling in of the gap, and, at the same time, it ought to consist of absorbable material which would allow itself to be disposed of by the tissues after its function had been performed. With this object in view an absorbable turkey-bone drainage tube was selected from the material most readily at hand.

A portion of the radial shaft $2\frac{5}{8}$ inches was removed and a turkey bone—decalcified—was introduced and fixed to either end of the remaining shaft. Blood clot quickly filled the inserted tube. New bone issued from the two divided ends of the shaft and gradually filled the decalcified tube. When the experiment terminated at the end of ten weeks, the decalcified tube was found to have become absorbed, and in its place there was a mass of fibrous tissue fixed, without to the ulna and muscular sheaths and within to new bone continuous with the radial shaft at both ends. The new bone had taken on somewhat the shape of the lumen of the turkey-bone tube,—it had been cast in the form of the interior of the mould—though the mould itself had disappeared soon after. But there was a thickening in the bone (not corresponding with the lumen of the tube) at the part where the new growths from either end of the shaft had met and pressed the tissues aside.

In human surgery decalcified bone tubes have been used successfully as an aid to osseous regeneration emanating from the diaphysis. Where defects have occurred in the shaft during the growing period of bone, such tubes introduced into the interior have temporarily maintained the distance between the divided ends of the bone and prevented the tissues from filling the gap by lateral pressure. The blood and serum with which they become filled offers a framework readily penetrated by the osteoblasts and abundant nutriment for their growth. The tube itself is readily absorbed.

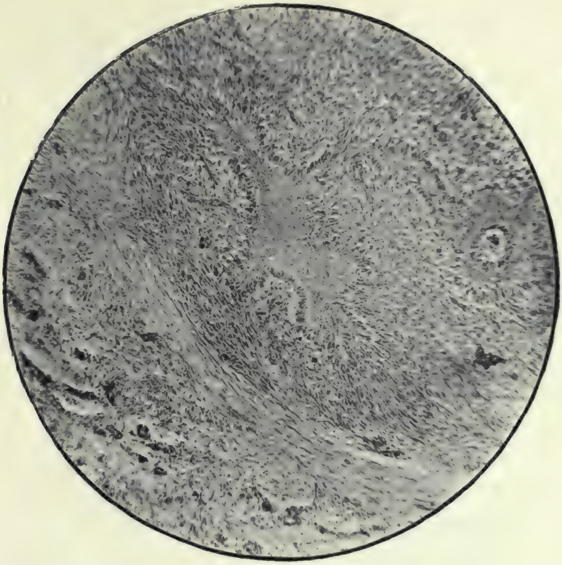
OSTEOBLASTS CARRIED BY BLOOD STREAM.

While endeavouring to produce experimentally the conveyance by the blood stream of minute particles of living bone or osteoblasts in process of generation, and, finding considerable difficulty in doing so, the following case presented itself which not only aptly illustrates the point desired but shows the beauty of Nature's work.

OSSEOUS WALL FORMED FROM OSTEOBLASTS DISTRIBUTED OVER THE SAC OF A FALSE ANEURISM.

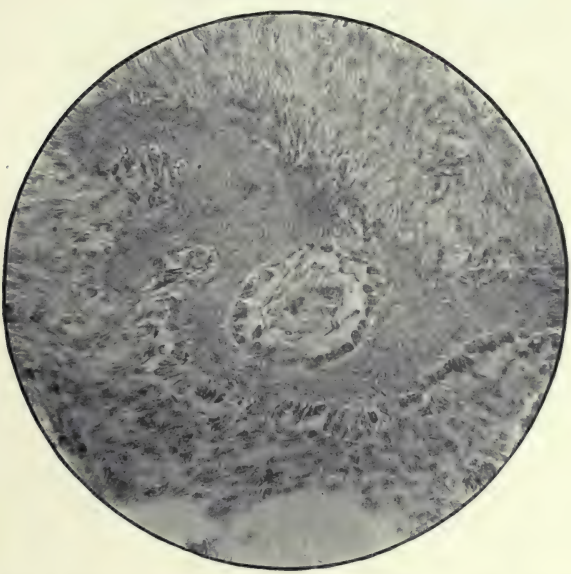
The specimen was obtained from the wall of a false aneurism which had formed by a puncture of the brachial artery. The shaft of the humerus had been fractured near its distal extremity by direct violence, and a spiculum from the interior of the fractured bone had penetrated the brachial artery near the elbow, a false aneurism ensuing. Six weeks after the injury the patient was seen by me with an aneurismal swelling about the size of an orange in front of the elbow. It was very dense and inelastic to the touch, and there was very little pulsation to be detected, though pulsation had been a marked feature in the early stages of

FIG. 32.—INITIAL STAGES OF OSTEOBLASTIC BONE FORMATION—SECOND GLASS TUBE EXPERIMENT.



One of the early appearances of osteoblastic bone formation within glass tube—seen in the centre of the field. The peripheral osteoblasts are in vigorous proliferation. ×24.

FIG. 33.—INITIAL STAGES OF OSTEOBLASTIC BONE FORMATION—SECOND GLASS TUBE EXPERIMENT.

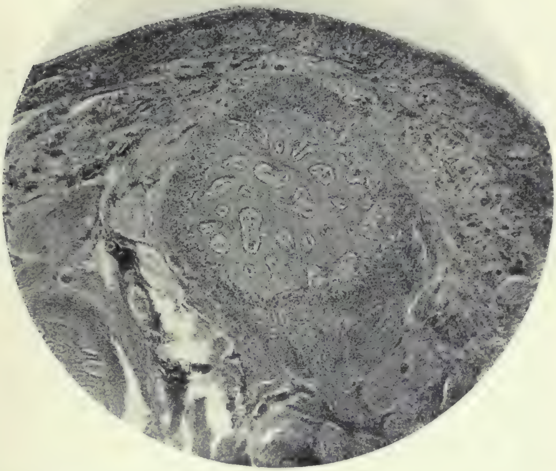


Island of bone in process of formation from osteoblasts which line the periphery and the interior of the circular space. The bone cells may be seen in the interior of the island. ×66.

FIG. 34.—EARLY BONE FORMATION—GLASS TUBE EXPERIMENT.

Bone forming in middle of osteoblasts. ×66.

FIG. 35.—EARLY STAGES OF OSTEOBLASTIC BONE FORMATION—SECOND GLASS TUBE EXPERIMENT.



More advanced bone formation in midst of granulation tissue and blood clot, and surrounded by a zone of osteoblasts which likewise line the circular spaces. ×24.

FIG. 36.—INITIAL STAGES OF BONE FORMATION—SECOND GLASS TUBE EXPERIMENT.

Further islands of bone formation. ×66.

the swelling. Flexion of the elbow was impossible owing to this obstruction. The aneurism was removed.

On operation it was found that the entire circumference of the wall of the false aneurism was formed by plaques of new osseous tissue. A few of these were continuous with a new formation of bone which had formed from a spiculum which had penetrated the brachial artery. The other and more numerous osseous plaques had evidently been formed by detached osteoblasts, which had emanated either from the spiculum or from the adjacent surface of the fracture and had been washed away from the osseous surface by the blood stream issuing from the punctured artery, and were deposited in the fibrin on the periphery of the sac.

The osteoblasts had evidently become peripherally distributed and entangled in the meshes of the fibrin formed in the coagulating blood. The interior of the sac was filled with fluid blood.

In order to preserve the surrounding soft structures, the wall of the aneurism had to be removed in pieces, and during this process several of the plaques of bone crumbled into little fragments and were lost. The specimen shows about two-thirds of the circumference of the aneurism (Fig. 37).

The structure of the osseous plaque is that of loose cancellated tissue, apparently built on a fibrinous framework such as might be met with in blood clot. From the eccentric manner of its growth it resembles the osseous formation in the interior of the blood clot in the glass-tube experiments.

The cure of the aneurism by the peripheral distribution and growth of bone was thus being carried out at the time of removal of the aneurism. Therapeutically this might be of service in the cure of aneurism. The

removal of the mass in this case was however necessary, not because it was aneurismal, but on account of the ever-increasing solidification of the mass restricting the power of movement of the elbow joint.

In this instance the osteoblasts were conveyed by the blood stream for a short distance only, measured by one or two inches, where they were caught in the meshes of the fibrin forming the wall of the false aneurism. Had the osteoblasts been washed into the interior of a blood vessel, they might have been carried by the blood stream and thus have produced osseous infarctions in the internal organs, or have been deposited in muscles, or even possibly have produced general dissemination.

In this connection it will at once occur to those familiar with the pathology of aneurism of the large vessels, especially the aorta, how frequently towards the last stages, part of the wall has been destroyed and the blood stream passes over bare bone without showing evidence of the dissemination of osseous particles throughout the body distributed by means of the blood stream. In such cases as these the conditions are not the same as the one here recorded. In the first place the structure of the vertebrae is cancellous tissue, which does not, in its adult condition, lend itself to prolific cell production. Secondly, the bone at the place where such aneurisms are situated is subject to pressure, and has already become partly absorbed, and is undergoing further absorption, and thirdly, the vitality of the organism as a whole is greatly diminished and does not show any indication of fresh cellular regeneration. Whereas the patient from whom this specimen was obtained is in full vigour of life, and the spiculum of bone is from the diaphysis of a long bone which throws out callus abundantly in the process of repair such as in the healing of fractures.

FIG. 37.—OSTEOBLASTS CARRIED TO A DISTANCE AND DISSEMINATED BY BLOOD STREAM. OSTEOBLASTS GROWING IN ANEURYSMAL SAC.

Osseous wall formed from osteoblasts distributed over the sac of a false aneurism which had resulted from puncture of brachial artery by spiculum of fractured humeral diaphysis.

It must be obvious that ossific production found in the blood clot of a false aneurism, the osteoblasts emanating from a naked spiculum of bone derived from the interior of the fractured shaft, could not have been produced from periosteum.

GROWTH OF BONE IN MUSCLE.

In the foregoing (and in some of the subsequent) observations attention has been called to the fact that muscles lying alongside of bone which had been bereft of its periosteum were apt to have the connective tissue surrounding their contiguous muscular fibres infiltrated with osteoblasts, and hence they became adherent to the fresh osseous layers forming on the outside of the shaft. This was more marked where the nude bone was introduced in the shape of small shavings and the muscles were made to surround them intimately, and more especially where the connective tissue covering of the muscle fibres and the muscle fibres themselves were lacerated. At such places the invasion of the osteoblasts was greater.

An instance of the growth of bone in the midst of torn muscle at a distance from the source of the osteoblastic supply, may be here given, as its history is known and it may throw light upon other cases of a similar kind.

OBSERVATIONS ON GROWTH OF BONE IN THE MUSCLES.

It occurred in a strong, healthy man, aged 34 years, who fell a short distance, the outside of his thigh striking against the edge of a steel plate. The femur was injured at its upper third, an indenture in the bone ensuing with the separation of a small portion of the shaft, but without destroying the continuity of the

femur as a whole; the deeper layers of the intervening soft tissues on the outside of the thigh were severely injured and infiltrated with blood, which caused a swelling of the thigh, increasing slowly during the first 24 hours. This compelled him to maintain the recumbent position for some weeks during which he had massage applied, first by himself, and when it was seen that the swelling was not being reduced sufficiently quickly to satisfy the patient, the massage was undertaken by some of his vigorous fellow-workmen, who had had "first-aid" lectures, and who continued it every night for some weeks.

Under this treatment the swelling subsided, and as it did so a hard lump was felt on the outside of the thigh not far from the skin as they thought. The patient was the first to notice the hard lump, and is positive that there was no such hard mass there before the injury. This was shown to the doctor who first examined the man after his accident, who at once detected it and said there was no such hard swelling there when he had first examined the limb before the thigh was swollen.

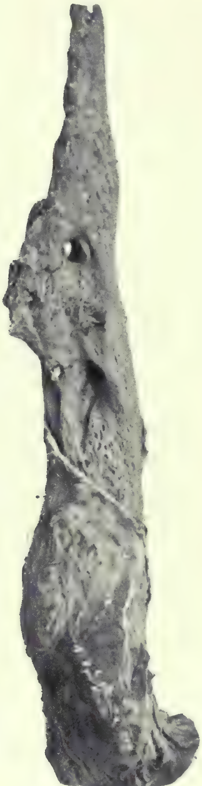
He examined the man fortnightly afterwards, and each time he found the osseous nodule increased in size. On the third occasion a second nodule was found on the upper part of the first nodule, and it also gradually increased in bulk. The man, however, though impeded in his movements, was able to work, and continued to do so until about nine months after the accident, when the bone mass, which had been growing all the time, had attained such a size that it greatly impeded him in walking and in his work. He was then sent by his medical attendant to me.

When examined by me there was on the outside of

FIG. 38.—BONE GROWN IN SOFT TISSUES.

Mass of bone, 7 inches long, growing in the injured muscular tissues of the thigh, from osteoblasts poured out from the femur. Showing tendons enveloped at its apical part.

FIG. 39.—BONE GROWN IN SOFT TISSUES.



Another view of same specimen, showing apertures in the new bone, through one of which a nerve, and through another of which a tendon, passed.

the thigh, in the situation of the vastus externus, and apparently under the fascia lata, a hard tumour of bony consistence, which seemed to extend from below the trochanter major to the lower third of the thigh. The tumour was movable on the underlying structures, though somewhat attached to the fascia lata. Although it now seemed to form a continuous tumour, the upper part moved on the lower, and the patient showed that when he sat the upper mass was in a different relation to the lower mass than that which it occupied when he stood up. It seemed flexed when he sat, and straight when he stood erect (Figs. 38, 39, 40 and 41).

During the operation it was seen that the osseous masses lay principally in the vastus externus under the fascia lata, and extended from a couple of inches below the tip of the trochanter major to within $3\frac{1}{2}$ inches from the condyles of the femur. They lay abutting each other, the upper measuring $3\frac{1}{2}$ inches in length, and, allowing for the false joint, the specimen measured 11 inches in length, and the lower one was 7 inches long—together they measured $10\frac{1}{2}$ inches long. The lower fragment was $1\frac{1}{2}$ inches at its greatest breadth, while the upper was $1\frac{1}{4}$ inches in breadth.

They were both under the fascia lata and the tensor vaginae femoris; some, however, of the fibres of the former fascia were caught in the interior of the bone; one elongated portion of the fascia was completely surrounded by bone.

Many muscular bundles of the vastus externus were included within the grasp of this ossific formation, which impeded their movement, while one passed through a tunnel in the bone through which it worked, and the sides of which were polished as if by the continual gliding muscular movement.

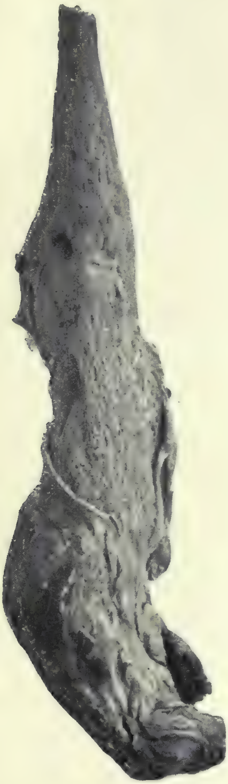
The structure was as a whole very vascular. There were several vessels of large calibre—one fully that of the radial in its upper third, which passed through apertures in the bone as if the osteoblasts had formed round these vessels, making an archway for their accommodation. Though these vessels contributed to the vascular supply of the new bone, they were distributed mainly to the soft parts, and one of them came directly from the vicinity of the femur.

The upper bone mass lay near the notch made by the injury in the femur, a portion of connective tissue separating the upper fragment from the bone. The lower mass was separated from the femur by muscular tissue, and nearer to the fascia lata.

It was interesting to see, at the part where the two newly-formed bones came in contact, that their surfaces fitted each other, and were polished and felt almost as smooth as if covered with cartilage. They were at this part surrounded by a capsule of fibrous tissue formed in strong bands, in one of which there was an osseous nodule somewhat like a sesamoid bone flattened like the patella in shape. The fibrous capsule, when opened, was seen to contain a thin serum, which, though not of the consistence of synovial fluid, still aided in lubricating the polished osseous surfaces as they played over one another. Here were the elements of a joint formation between these two newly-formed bones which had grown in the midst of the muscles.

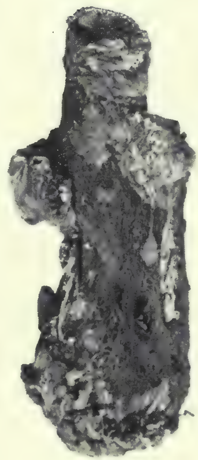
Note.—A somewhat similar instance was seen by Dr. P. Paterson, surgeon, Glasgow Royal Infirmary, in which the specimen, though much smaller than the above, was found in the muscles of the thigh after injury to the femur, though the new bone in Dr. Paterson's case was attached in two places to the femur.

FIG. 40.—BONE GROWN IN SOFT TISSUES.



Back view of same specimen, showing two apertures, through the lower of which a tendon still continued to play, and through the upper an artery passed—both having become enveloped in bone.

FIG. 41.—BONE GROWN IN SOFT TISSUES.



Upper portion of bone growing in muscles of thigh and united to lower by a new-formed joint.

Another case of a new growth in muscle occurring after injury was found by Dr. Paterson in one of the muscles of the upper arm. (Brachialis anticus.)

Comments.—Here was a case of limited injury to the bone, causing an indentation in the shaft with the detachment of a small portion of the femur. This was accompanied by laceration of the muscles under the fascia lata, and by extravasation of blood. The fascia lata here acted as a limiting membrane. The osteoblasts poured out from the osseous hiatus, and from the small fragment of the femur escaped into the surrounding tissues, where they probably would have formed a nodule of bone cementing the detached fragment to the femur.

The osteoblasts were not however allowed to remain at rest in their normal position, but were scattered broadcast among the injured tissues by the vigorous massage of the "first-aid"-taught workmen. The extravasated blood, while holding the injured tissues apart, afforded easy penetrability to the osteoblasts and supplied temporary pabulum, which was augmented by contact with the blood vessels of the part.

If a strip of periosteum, while retaining its blood supply, be partially detached from the bone and carries osteoblasts or bone plaques with it, bone nodules may form from the proliferation of such detached osteoblasts; but it would be wrong to deduce therefrom that the periosteum was the generator of those osteoblasts.

Tendons which are directly inserted into bone, without the intermediary of the periosteum, are, under exceptional circumstances, liable to osseous infiltration. When such tendons are subject to violent strain, this is transmitted to the bone in which they are inserted. The traumatism thus produced loosens the tissues, and

the mechanical irritation causes a proliferation of osteoblasts, which penetrate the partially ruptured, loosened and retracted fibres of the tendon, and set up ossification in their midst. Some of the fibres of the tendon, which were in contact with the bone, after rupture may retract into the tendon, carrying osteoblasts from their point of insertion. Rider's bone results in this way.

Is it possible that, after injury or other cause of osteoblastic proliferation, the osteoblasts, under very exceptional circumstances, may gain access to the lymph or blood vessels, and be carried to and deposited in distant parts, where ossification may be established from proliferation of the cells? It is probable that some forms of myositis ossificans may be thus produced. Many cases of myositis ossificans occur subsequently to an injury in which the bones are involved.

The muscles, when healthy, unimpaired and intact, seem to have the power of resisting osteoblastic invasion, though the osteoblasts, when freed from their limiting membrane, penetrate the loose areolar tissue in the neighbourhood of the muscles, and so form partial adhesion to the muscles which are at least sufficient to impair or restrict their movements. (As these are slight, massage, passive or voluntary movements are usually sufficient to restore the function.) When, however, the muscles are bruised, torn, or lacerated, and more especially when ruptured and infiltrated with blood, the osteoblasts are apt to penetrate the injured muscle and to surround the torn fasciculi, which ultimately become imbedded in osseous tissue. Much movement of the injured parts during the early period of osteoblastic invasion is apt to disseminate the osteoblasts and cause further fixation of the torn muscles, although the maintenance of movement may mould the ossific pro-

duction and thus prevent impairment of function. The outpouring of blood from the bone and other injured tissue acts as a vehicle for the distribution of the osteoblasts, the blood serum supplies them with pabulum, and the loose, easily penetrated fabric furnished by the subsequent coagulum enables the osteoblasts to regenerate with rapidity and probably with greater freedom than would obtain inside of the limiting membrane.

Other structures, such as tendons, arteries, and nerves, may also be surrounded by the disseminated osteoblasts, which then form a firm osseous framework round them.

Osteoblasts infiltrating Muscles.—In the course of these experiments, it has been many times noted that where a fresh development of ossific matter has been poured out, the adjacent muscles, especially when ruptured or lacerated and filled with blood and plastic effusion, are apt to be infiltrated by the overflowing osteoblasts, and the muscular fasciculi become embraced in the rigid grip of the new formation of bone. This is seen clinically after fractures and other lesions where fresh depositions of bone take place peripherally.

OSTEOBLASTS ENVELOPING MUSCULAR FASCICULI AND TENDONS.

Experiment Z.—In the case from which the specimen figured was obtained, a portion of the whole circumference of the shaft was removed along with its periosteum, and the hiatus thus left became filled by new osseous tissue thrown out from both ends of the diaphyses. During this process, the osteoblasts having been freely poured out, and being aided by the subsequent muscular movement, the adjacent muscular fasciculi and tendons and the fibrous tissue surrounding

them became infiltrated and surrounded and finally grasped by the solidifying bone. The specimen does not show the whole osseous entanglement of the muscles, as these for the most part were removed along with some of the soft superficial bone, in order to show clearly what remains (Figs. 42 and 43).

OSSEOUS REGENERATION IN FLAT BONES.

Cancellous tissue heals well but sparingly, with little excess over what is required—unless under special stimulation. Regeneration of osseous tissue from flat bones is less vigorous than that from the diaphyses. In the flat bones of the skull this is especially noticeable, and it is wisely ordered, as pressure upon the cranial contents from callus might otherwise ensue after many fractures. Doubtless this is aided by accurate coaptation and by the fact that many fractures are only fissured.

MOSAIC WORK OF RE-IMPLANTED BONE IN SKULL.

Can a flat bone, such as those of the cranial vault, continue to grow and its elements proliferate after it has been deprived of its periosteum and has been re-implanted? There have been many opportunities of testing this, from which the following observation may be cited:

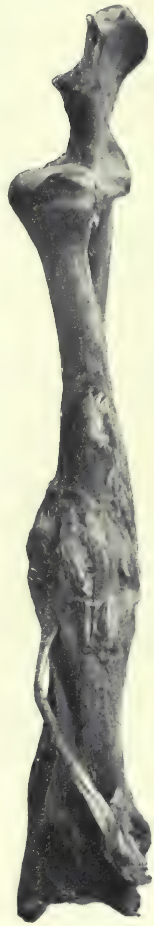
A weak, ill-fed boy, aet. 9 years, was admitted into Ward 29, Glasgow Royal Infirmary, in January, 1884, suffering from a compound comminuted fracture of the skull, with penetration of the brain substance, received about two hours previously by the fall of debris from a chimney. The brain symptoms are not referred to here.

There was a wound situated over the left side of the

FIG. 42.—TENDONS AND MUSCLES ENTANGLED IN NEW BONE FORMATION.

Front view.—Removal of one inch of whole circumference of radius along with its periosteum. The specimen shows the osseous gap filled by diaphyseal growth, and the entanglement of the adjacent muscles and tendons by the new bone formed by the out-poured osteoblasts.

FIG. 43.—TENDONS AND MUSCLES ENTANGLED IN NEW BONE FORMATION.



Side view.—Showing tendon grasped and fixed by new ossific production.

head of a somewhat crescentic shape, and extending from above the middle of the left eyebrow to an inch behind the auriculobregmatic line. The scalp was torn into several pieces, some of which lay over the ear. All of them were much bruised and lacerated.

The skull was found shattered from an inch above the middle of the left eyebrow to a point half an inch behind the auriculobregmatic line. The depressed portion was somewhat elliptical, with very irregular margins. It measured, at its broadest part, 2½ inches. All of these portions of bone were depressed below the level of the skull, most of them having penetrated the brain membranes into the brain tissue. These portions of bone were all elevated. It was found that they consisted of 11 pieces, the periosteum having been scraped by the injury from all of these, with the exception of the most posterior one, which was only partially denuded. Many of them were infiltrated with lime debris, brick-dust, etc.

These pieces, as they were elevated, were placed in an aseptic solution. They were then pared with a chisel in order to remove the debris. This was especially necessary over the external surface, where they had been scraped and ingrained with dirt. They were afterwards thoroughly washed in an aseptic solution, divided into fragments and replaced. In this way a mosaic work of 14 pieces of bone was formed. It was difficult to retain these in position owing to four things. First, to the extent of the osseous defect; second, to the fact that the dura mater had been so extensively lacerated and torn that it formed a very irregular floor to rest the fragments upon; third, to the great bruising and crushing of the scalp, which rendered it difficult to bring the several pieces into apposition and made sloughing of a

part of it almost certain; and fourthly, to the force of the cerebral impulses, which acting through the torn dura caused a distinct movement of the fragments, producing crepitation by the one rubbing against the other. It was feared that, owing to these four circumstances, some of the fragments would be shed (Fig. 44).

It is to be borne in mind that the periosteum had been by the injury entirely removed from all these fragments, except the most posterior one, and that most of them had to have their external surface pared with a chisel. The soft tissues were brought together as well as possible, and the wound was dressed.

On the sixth day after the operation the wound was examined. A portion of the anterior aspect of the flap, which was lacerated and contused, had sloughed, and already the process of separation from the living part had commenced. On the tenth day the wound was re-examined, and this portion of the slough was removed. It was then seen that four fragments of bone were exposed, two of which lay side by side and presented a striking contrast. The one was suffused with the pinkish blush of life, the other with the pallor of death.

The condition of the remaining exposed fragments was doubtful, one of them, however, being very pale. On the 21st day, at the next dressing, two pieces of bone were found to have been shed while all the remainder had lived. The wound was all but healed. At the termination of a month it was firm (Fig. 45).

Had that large osseous defect, about 2½ inches in greatest breadth, extending from the middle of the left eyebrow to the auriculobregmatic line, been left without this mosaic work of re-implanted bone, the cranial periosteum, if any of it was left at that part, would

FIG. 44.—OSSEOUS REGENERATION IN FLAT BONES—SKULL.

Schema of re-implanted portions of skull.

FIG. 45.—OSSEOUS REGENERATION IN FLAT BONES.

Mosaic work of bones of skull by re-implantation. Boy aged 9 years—result when completed.

have failed to have covered the defect with bone, and a permanent fibrous covering transmitting the cerebral impulse would have marked the seat of injury. Yet, here we re-implant the osseous fragments, and the majority of them live, grow, and throw out ossific matter sufficient to unite them individually to one another and to the rest of the uninjured cranium.

Ten years after this operation, the lad was examined. He was then 19 years old, strong and robust. The skull was firm all over, the bones over the site of prior injury had grown in proportion with the rest of the skull.

THE RESULT OF HUMAN RE-IMPLANTATION IN ONE OF THE FLAT BONES OF THE SKULL—THE PARIETAL—AND EVIDENCE OF FRESH OSSEOUS GROWTH THEREFROM.

The two accompanying photos show the result of human re-implantation of one of the flat bones of the skull—the parietal—five years after the operation. The operation was for the relief of cystic intra-cranial disease, which was successful. Five years subsequently, the patient died from pulmonary haemorrhage. The specimen does not show the result of an osteoplastic flap, but a portion of bone which at operation was elevated and removed from the skull, preserved in warm, sterilised salt solution during half an hour and then re-implanted and held in position by sutures, which in this case were required by reason of the gap left by the compressed brain.

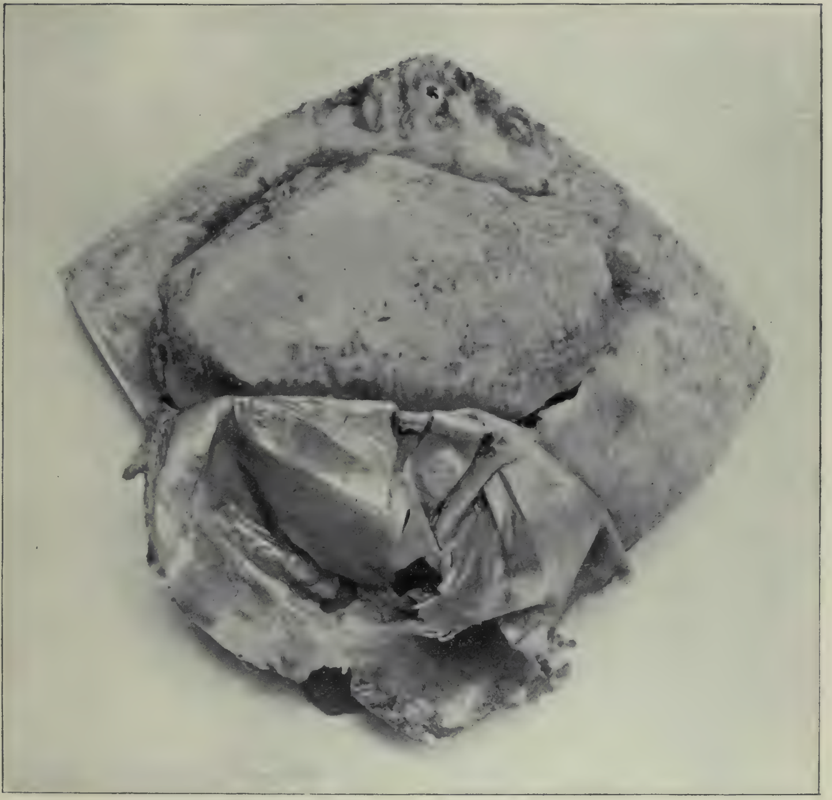
In process of removal, a gap of quarter of an inch in breadth was made by the bur in the entire periphery of the bone. The specimen shows that this gap has been filled by the growth of fresh osseous tissue for over three-quarters of its circumference, firm osseous union

occurring between the re-implanted bone and the skull (Figs. 46 and 47).

Over the lower border there is a gap which is filled by fibrous tissue. This was a part from which an extra portion of bone was removed and which was not re-implanted owing to the desire to secure drainage of the cavity left by the cyst in the brain.

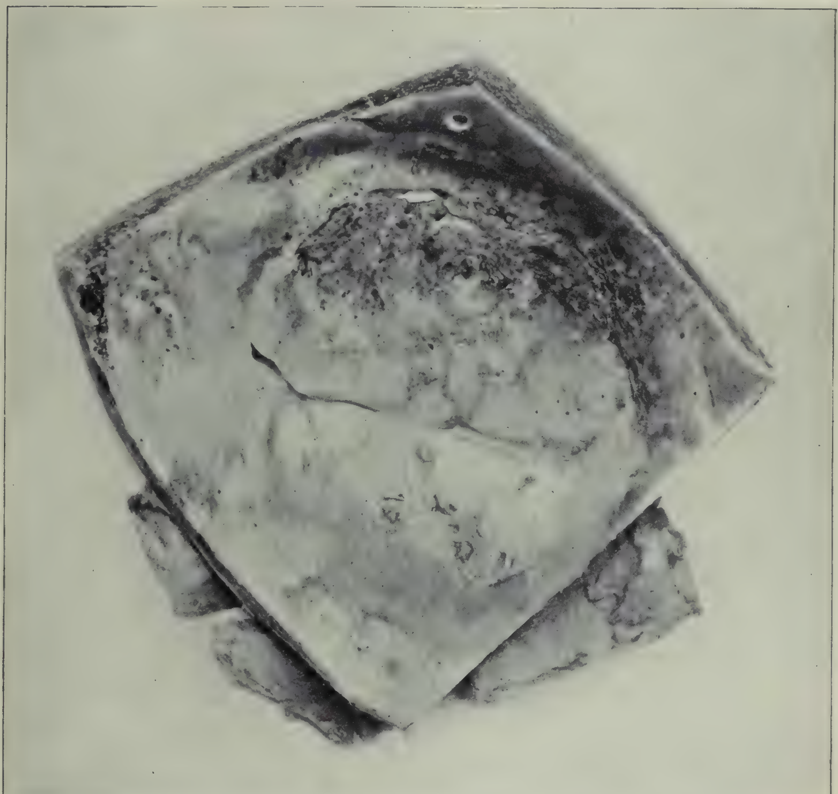
This case is given merely as an illustration of many cases in which portions of bone have been re-implanted in the skull and have succeeded in forming firm osseous union with the neighbouring bone.

FIG. 46.—RE-IMPLANTED FLAT BONE—SKULL. OUTSIDE VIEW.



Re-implanted parietal bone—result 5 years after—showing regeneration of bone in the osseous union extending over the greater part of its periphery; a fresh formed fibrous tissue covering is reflected, except at its lower part.

FIG. 47.—RE-IMPLANTED FLAT BONE—SKULL. INSIDE VIEW.



Re-implanted parietal bone 5 years after, showing regeneration of bone in the osseous union of periphery and a fibrous union at lower border.

CHAPTER V.

THE OSTEOGENIC POWER OF THE EPIPHYSEAL CARTILAGINOUS PLATES IN REGENERATION OF BONE.

THE DIAPHYSIS REMOVED SUBPERIOSTEALLY, THE PROXIMAL EPIPHYSIS BEING DAMAGED WHILE THE DISTAL EPIPHYSIS WAS LEFT INTACT.

Experiment Q.—(1) To test the power of the epiphyseal cartilaginous plates, to reproduce bone to fill up a gap in the shaft.

(2) And secondly, to test the power of the periosteum to regenerate bone.

The shaft of the right radius was removed subperiosteally from one epiphyseal cartilage to the other. A small amount of bone, about quarter of an inch in linear extent, was allowed to remain on the diaphyseal side of the cartilage to ensure the vitality of the cartilaginous plate.

In process of removal of the shaft, the head of the radius became partially detached, so that it hung by synovial membrane and periosteum only. The blood supply to the proximal epiphysis was thus markedly interfered with. This fact requires to be considered in estimating the result of the relative growth from the two epiphyses.

Result 6 *Weeks after.*—The ulna has bent owing to the weight of the body. The radial shaft has been reformed, but not as normal.

The growth of bone from the unimpaired distal epiphyses is strong and vigorous, while that from the injured proximal epiphyses is very attenuated and in marked contrast with the growth from the lower end (Fig. 48).

Comment.—Had the periosteum been the source of bone reproduction, it would have produced the bone of the shaft equally throughout, and a uniform osseous development as great in the centre as at either end would have resulted.

The specimen therefore shows that the periosteum did not share in the osseous reproduction. The osseous tissue that restored the shaft grew from the epiphyseal lines; strong and robust from the uninjured epiphysis, and weak and attenuated from the one which was injured and whose blood supply had been seriously interfered with.

Normally the distal radial epiphysis is the one which is the more vigorous and prolific in osseous growth, but in this case the growth from the proximal end of the shaft was markedly deficient, and this deficiency could only be accounted for by the impairment of the vitality of the proximal epiphysis.

METAL CAPS PLACED ON THE DIVIDED EXTREMITIES OF THE SHAFT ON THE DIAPHYSEAL SIDE OF THE EPIPHYSEAL CARTILAGES WHILE THE REMAINDER OF THE SHAFT WAS REMOVED.

Experiment X.—To test the power of the epiphyseal plate of the diaphyses to fill a gap in the shaft, and the relative potency of the periosteum and bone shavings transplanted into the soft tissues of the neck, to reproduce bone in these situations—heterotopic transplantation.

From a radius four inches long a portion of the shaft

FIG. 48.—TO TEST THE POWER OF THE EPIPHYSEAL CARTILAGINOUS PLATES TO REPRODUCE BONE AFTER REMOVAL OF THE DIAPHYSIS.

Result 6 weeks after.—Vigorous growth from uninjured distal epiphysis. Dwarfed growth from injured proximal epiphysis. No evidence of osseous reproduction from periosteum, as if so, it would have reproduced the shaft equally.

was removed, measuring two and a half inches in length. Thus the epiphyseal cartilaginous plates were left intact and a small portion of the shaft on the proximal and distal side of the epiphyseal plates.

(1) After excision of the bone, the periosteum was stripped off from it in one piece and placed in the neck, surrounding, for two thirds of its circumference, the left external jugular vein. This piece measured two and a quarter inches in length by half an inch in breadth—it had contracted quarter of an inch after removal.

(2) Two shavings of bone, half an inch long and one-eighth in breadth, were then removed from the denuded bone and placed in the midst of fatty and connective tissue on the right side of the neck near the trachea.

(3) Two metal caps were then placed on either extremity of the small portions of the shaft, still remaining *in situ*, so as to completely cover their cut surfaces and to pass for fully quarter of an inch over either end of the shaft abutting on the epiphyseal lines.

The periosteum for two and a half inches had been entirely removed along with the shaft.

The operation was almost bloodless, and healing was aseptic—under one dressing.

Seven weeks after the specimen was examined.

(1) The gap in the shaft of the right radius, from which two and a half inches of the diaphyses, covered with its periosteum, was removed, was found to be completely filled with dense bone growing from either epiphyseal plate. At a point where the ulna had curved there was a mass of bone projecting from the lower portion of the diaphysis of the radius into the ulnar curve, and the ensuing pressure had caused absorption of the ulna at that point. Owing to the curve of the ulna the growing mass of bone from the

radial diaphyses had not been kept in a straight line—but was deflected. This deflection caused the extremities of the growing shaft to overlap and the metal caps which were carried forward by the growing bone, and which otherwise would have come in contact end to end, have consequently been placed laterally to one another (Figs. 49 and 50).

There is, however, a dense mass of new bone projecting laterally between and joining the two extremities of the shaft. This may be regarded as an overflow of bone poured out in order to escape from the confining influence of the metal caps which did not allow for circumferential expansion.

The result shows that the growth from the epiphyseal plate has been such as to push the metal caps forward at least an inch and a quarter from either extremity—$2\frac{1}{2}$ inches in all—during the six weeks, and, had it not been for the deflection in the ulna, they would have been found in end to end contact in the centre.

The metal caps themselves had become surrounded by a fine fibrous tissue capsule. There was no bone deposited outside of them, showing that the new connective tissue and muscular structures which surrounded them, in the absence of the periosteum, had not the power of depositing osseous tissue.

(2) The layer of periosteum, $2\frac{1}{4}$ inches in length, which was made to partially surround the external jugular vein had disappeared, except a hard nodule about the size of a pea which was found at one extremity. When examined microscopically, this nodule was found to consist of dense fibrous tissue with a kernel of ossified tissue about the size of a lentil.

Comment.—This particle of new bone which was found at one extremity of a portion of periosteum,

FIG. 49.—EPIPHYSEAL CARTILAGINOUS PLATES—THEIR OSTEOGENIC POWER.

(1) *Front view.*—From a shaft of radius 4 in. long, 2½ in. of shaft were removed (quarter of an inch from either epiphyseal line), with its periosteum intact. Metal caps were then placed on the shafts covering their cut extremities.

Result 7 weeks after.—The metal caps have been carried forward by the growth of bone to within half an inch of each other. They would have met together had it not been for the deflection in position, owing to the bending of the ulna.

FIG. 50.—EPIPHYSEAL CARTILAGINOUS PLATES—THEIR OSTEOGENIC POWER.

(2) *Back view.*—Same as Fig. 49. Showing continuous osseous formation in shaft.

measuring $2\frac{1}{4}$ inches, must have emanated from some minute osseous flake or group of osteoblasts adhering to the periosteum at the time of removal from the bone. Had it emanated from the periosteum, the whole length of the periosteal flap would have produced bone over its $2\frac{1}{4}$ inches.

(3) The two osseous shavings, bereft of periosteum, each about half an inch long and over one-sixteenth of an inch in breadth, which were placed in the soft tissues on the right side of the neck had grown together, so as to form in the soft tissues one plaque of firm, dense bone three quarters of an inch long and fully quarter of an inch broad by an eighth in thickness. The edges of this plaque showed evidence of active osteoplastic growth.

Comment.—It has been advanced by way of criticism to other experiments that the periosteum which had been left on the portions of the shaft which remained would take on an active proliferation and extend on both sides, so as to cover the intervening space between the epiphyses left by the removal of the bone and the periosteum. Hence this reproduced periosteum might have deposited the bone which would have constituted the new shaft. If this contention were correct, then, in this experiment, the two metal caps, instead of being carried so far forward by the growing bone, would have remained at short distances from the epiphyses, the interspace between them being filled with new bone from the periosteum, which would likewise have covered the metal caps with new bone, and which would have prevented them moving towards the centre. But neither of these followed, the experiment showing the reverse to have resulted—the new growth coming from the epiphyses and not from "reproduced periosteum."

THE OSTEOGENIC POWER OF THE DIAPHYSIS AND EPIPHYSIS BEREFT OF THEIR INTERMEDIATE CARTILAGINOUS PLATE.

Experiment A I.—Removal of the distal epiphyseal cartilage from the right radius while leaving the epiphysis and diaphysis intact. The object was to test the osteogenic power of the diaphysis and epiphysis bereft of their intermediate cartilaginous plate.

The inception of this project was easier than its execution. The removal through a single linear incision in the soft parts of the cartilaginous plate without damaging the epiphysis or diaphysis on either side was difficult, and in practice, both adjacent sides of the bone were interfered with, and possibly some small portions of the epiphyseal cartilage remained—though none were observed.

Aseptic healing ensued. After a few weeks it became apparent that the bones operated on were not increasing in length at the same rate as their neighbours on the left limb, and that there was a deviation in the articular surface of the radius as the paw was held obliquely.

Result 12 weeks after.—When the specimen was obtained, it was seen that the right radius and ulna had become fused together at their distal extremity. A quantity of diaphyseal bone had been pressed out from the line of section of the radius and had become attached to the shaft of the ulna from just above the epiphyseal line to near the tip of its distal epiphysis. The osseous soldering had produced complete anchylosis or fusion of the two bones at that point. The radial articular facet had become twisted toward the ulna from the unequal growth of the radial diaphysis—hence the deflected position of the paw (Figs. 51 and 52).

The right radius *and ulna* were markedly shorter

FIG. 51.—REMOVAL OF DISTAL RADIAL EPIPHYSEAL CARTILAGE.

Result 12 weeks after.—Showing growth of bone from sectioned surface of shaft causing deflection of articular facet and soldering of both bones and the epiphysis. Marked linear shortening of both bones.

FIG. 52.—REMOVAL OF DISTAL RADIAL EPIPHYSEAL CARTILAGE.

The same, posterior view.

than the corresponding bones on the left limb, the actual measurements being:

The right radius, - -	$4\frac{5}{8}$ ins.	
The left radius, - -	$5\frac{5}{8}$ „	almost.

The ulna, which had not been operated on, had participated in the decrease in length. The measurements were:

The right ulna, - - -	$5\frac{5}{8}$ ins.
The left ulna, - - -	$6\frac{5}{8}$ „

so that there was here an inch of shortening which had resulted, in three months, from the removal of the epiphyseal cartilage. At the same time, it was apparent that there was an increase in breadth of the lower third of the right radial diaphysis when compared with that of the left radius.

It is to be remembered in considering these measurements that at least $\frac{1}{8}$ in. of length of shaft was removed in taking away the epiphyseal line of radius.

Comment.—Twelve weeks after the excision of the epiphyseal cartilage from the right radius there resulted:

1. An inch of shortening of both radius and ulna.
2. An abnormal thickening of the radius.
3. The radial diaphyseal osteoblasts, rapidly proliferated and having no limiting membrane to confine them, were poured out from the freshly sectioned surface of the shaft into and through the gap left by the removal of the epiphyseal cartilage.
4. In consequence of the latter, and the fact that the diaphyseal osteoblasts were poured out unequally, the radial epiphysis was twisted so that its articular facet, instead of looking downwards, was turned toward the ulnar side. This is in a physical sense somewhat similar

to the wedge-shaped diaphyseal increase which occurs on the inner side of the human femur, causing one of the forms of genu valgum.

5. Also in consequence of No. 3 the radius became firmly soldered to the ulna.

6. The epiphyseal cartilage having disappeared, soldering of the epiphysis to the diaphysis ensued. This took place after the outpouring of the osteoblasts.

7. Subsequent to the soldering of the epiphysis, the fact that the shaft increased in thickness in its lower two-thirds was interpreted as evidence that there remained in the shaft an interstitial osteogenic potency which, being checked in one direction, expanded itself in another. The expansion in breadth was not, however, quite commensurate with its loss in length.

8. The mass of outpoured osteoblasts emanating from the shaft bereft of its epiphyseal cartilage was great in proportion to the length of the shaft. If this mass could have been retained within the line of the shaft, the shortening which had occurred before consolidation had taken place would have been materially lessened. The amount of osteoblastic outpouring could have been greatly increased had the osteoblasts been distributed and had their ossification been retarded. Once they became ossified to one another and to the shaft the further escape of osteoblasts was prevented and soldering occurred which retarded further growth in length from the distal epiphysis.

9. The check to the growth in length of the neighbouring bone—the ulna—was apparently due to a mechanical cause, the fixation of the distal portion of the shaft and the epiphysis of the ulna by osseous anchylosis to the radius which prevented linear expansion. It demonstrated that extraneous fixation of the epiphysis to

FIG. 53.—REMOVAL OF DISTAL RADIAL EPIPHYSIS AND EPIPHYSEAL CARTILAGE.

Result 12 *weeks after*.—Showing new bone from sectioned radial diaphysis uniting with ulnar epiphysis. Marked shortening of both shafts.

the diaphysis can interfere with or prevent normal linear growth. The bearing of this in human surgery is evident, and may explain other obscure epiphyseal problems.

THE REMOVAL OF THE DISTAL EPIPHYSIS AND THE EPIPHYSEAL PLATE TO TEST THE POWER OF LINEAR EXPANSION OF THE LOWER EXTREMITY OF THE SHAFT.

Experiment A II.—Removal of the distal epiphyseal cartilage along with the whole of the epiphysis. The carpal joint was necessarily opened in this experiment, the object of which was to test the power of the diaphysis to increase in length, apart from the epiphyseal plate and the epiphysis.

Aseptic healing ensued.

Result 12 weeks after.—The radius and ulna had become fused from diaphyseal osteoblastic formation issuing from the former, though in this instance the radial attachment was only to the epiphysis of the ulna distal to the epiphyseal line—the growing ulnar cartilage remaining free (Figs. 53 and 54).

Marked shortening of both radius and ulna ensued. The measurements of the bones on the corresponding sides being:

Right radius, -	- -	$4\frac{5}{8}$ ins. long.
Left radius, -	- -	$5\frac{7}{8}$ „

That is one and a quarter inch of shortening on the operated radius.

From this one requires to deduct the length of epiphysis and epiphyseal line which were removed—fully half an inch.

The right ulna,	- -	$6\frac{1}{4}$ ins. long.
The left ulna,	- -	7 „

The articulation of the head of the radius to the ulna had altered. The ligaments had become stretched and

the head of the radius lay partly at the lower border of the articular facet and partly on the shaft of the ulna below the facet. The ulnar radial facet appeared to have grown upwards away from the radial head, so that the ulnar radial articular surface was for the most part empty.

Comment.—The same phenomena had occurred after this experiment as after the previous one—the diaphyseal osteoblasts escaped from the sectioned surface of the shaft and formed an obtuse terminal mass with a polished surface from contact with the carpal bones. Some of the escaping osseous matter from the radial diaphysis had become fixed to the ulnar epiphysis, where it held it, in a rigid grip, which prevented the ulna from linear expansion in a downward direction. The ossifying force within the ulna, at its epiphyseal line, had tried to overcome this mechanical obstacle by continuing its distal deposition of ossific matter, expanding the shaft in the only direction which was partly free, and thereby pushing the shaft *proximally*, and hence the articular radial facet was moved upwards away from the fixed radius and the radial facet remained for the most part empty. Were this occurring in the human elbow the function of the joint would be markedly affected, the primary lesion being in the radial epiphysis.

There is evidence of growth of bone in the shaft after the epiphysis has been removed along with the epiphyseal line. The diaphyseal osteoblasts showed evidence of vigorous proliferation, though owing to carpal pressure they were forced out latterly, forming a mass which became adherent to the ulnar epiphysis. If this mass could have been placed longitudinally the shortening would have been much diminished. The rapid consolidation of this mass prevented further elongation.

FIG. 54.—REMOVAL OF DISTAL RADIAL EPIPHYSIS AND EPIPHYSEAL CARTILAGE.

Result 12 weeks after.—Side view, showing unoccupied proximal radial articular facet on ulna.

JOHN HUNTER'S EXPERIMENT ON DIAPHYSEAL GROWTH.

Data Bearing on the Increase in Length and Breadth of Human Bone.—Reference may be made to the deductions drawn by John Hunter from an experiment performed by him on one of the lower animals. He bored two holes in the tibia of a young pig, one near the upper end and the other near the lower; the space between the holes was exactly 2 inches. A small leaden shot was inserted into each hole. When the bone had increased in length by the growth of the animal, the pig was killed and the space between the shot was still the same, exactly 2 inches. He inferred that "bones are not elongated by new matter being interposed in the interstices of the old." Probably what he meant was that new additions of bone are made to the length of the diaphysis from either epiphysis.

HUMAN EPIPHYSEAL GROWTH, AS SEEN AFTER INTERHUMAN TRANSPLANTATION.

The evidences of human epiphyseal growth are in a broad way similar to those found in the lower animals. Corroboration of this may be seen in numerous directions. The explanation of the formation of conical stump occurring years after the performance of amputation in early childhood through the middle of one of the long bones—femur or humerus—is due to the continuance of epiphyseal growth. In such a case the muscles retract from disuse atrophy while the bone continues to grow in length from the proximal epiphysis, and consequently soon exerts pressure on the face of the flaps, stretching them forward, thinning them, then causing pressure absorption, which ultimately permits the bone to push itself through the skin—often as it does so, however, it becomes clothed with a thin pellicle

of epithelium. Direct demonstrable evidence of human epiphyseal growth, apart from interstitial, is not easily obtained. In order to demonstrate the evidence of human epiphyseal growth an instance of interhuman transplantation is here adduced, in which the transplanted portions of bone have been altered in their relations to the proximal epiphysis, from which the new bone grew.

The Result of Epiphyseal Growth in Man, as seen Thirty Years after Interhuman Transplantation of Bone.—W. C., aged 3 years, was admitted into the Royal Infirmary, Glasgow, under my care on July 17, 1878, in an emaciated and exhausted condition from suppuration in connection with necrosis of the right humerus, evidently from osteomyelitis.

He presented the appearance of a much neglected child. The right arm was greatly distended and fluctuant from shoulder to elbow. An incision gave vent to fourteen ounces of thin, fetid pus. When the abscess was evacuated, the shaft of the humerus was found to be totally necrosed and already separated from its head near its epiphyseal junction. At the condylar epiphysis crepitation was likewise elicited. The bone was dark coloured and fetid (Fig. 55).

The arm was dressed and the patient was placed on a generous diet and otherwise attended to, in the hope that his strength might improve and that he would thereby be placed in a better condition for the removal of the necrosed shaft. Notwithstanding the treatment, the daily discharge of fetid pus was great, and as the amount was not much lessened at the end of three weeks, it was considered advisable to remove the source of irritation. This was done about nine weeks after the onset of the disease.

FIGS. 55, 56, 57.—SCHEMATA OF HUMERUS, SHOWING :

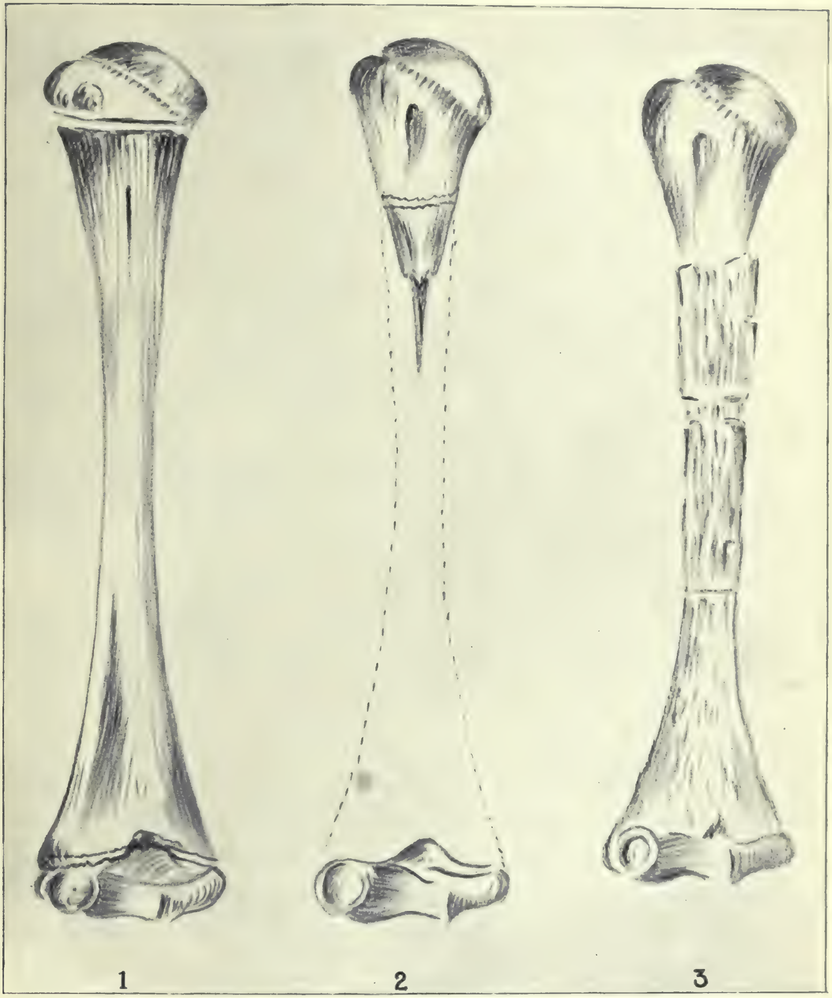


FIG. 55.
The diaphysis which was necrosed and removed.

FIG. 56.
The result 15 months subsequently, showing absence of shaft.

FIG. 57.
Result of the completion of the grafts.

The exposed loose bone was divided near its centre into two parts which were consecutively withdrawn. The two portions removed comprised the whole humeral diaphysis. The periosteal tube which remained was lined with a thick layer of granulation tissue which was soft throughout except at the proximal extremity, where the finger introduced into the tunnel detected rough, osseous plaques of bone. This tunnel was stuffed with carbolised lint and the arm was fixed on a splint. The tunnel left by the withdrawal of the bone gradually coalesced from the epiphyses toward the superficial openings without the formation of new bone, except for a short distance from the head of the humerus, where about an inch and a half of shaft had formed three months after removal of the dead shaft.

Four months after the removal of the necrosed diaphysis, a spike-like terminal extremity was found attached to the proximal portion. The measurement from the acromion process to the end of this tapered process was two inches. From the whole of the remainder there was no osseous deposition. He was seen monthly for some time, but no further growth of bone followed (Fig. 56).

Fifteen months subsequently he returned to the hospital, his parents desiring that the arm should be removed, as they said it was "worse than useless," inasmuch as he required the other arm and hand to look after the flail-like one which was constantly dangling loosely by his side. The condition of the arm was then as follows:

The bone showed no definite increase since he had left the hospital. When the limb was allowed to hang by his side, the measurement of the proximal portion of the humerus, taken from the acromion process to the distal

extremity of the proximal portion, was nearly two inches. In form, the proximal fragment was conical, tapering from the rounded head to a narrow, spike-like extremity. From this to the condyles there was a complete absence of bone, there being nothing but soft tissues in the gap. The muscular power was good, but when he attempted to raise his arm a contraction of the muscles took place, the condyles being drawn toward the proximal extremity, while some fibres of the deltoid raised the spike-like process of the upper portion, causing it to project as if about to penetrate the skin. Here the action ceased, the soft parts in the gap appearing like a rope during the muscular contraction. He could not raise his forearm to his breast. If one caught his arm firmly with the hand placed over the gap, so as to keep the condyles fixed and separate from the upper fragments, then the patient could elevate his forearm toward the chin. The power was there, the lever and fulcrum were wanting. It was determined to supply these by transplantation from other human bones.

In the wards there were numerous cases of marked anterior tibial curves, from which—in order to rectify their deformity—wedges of bone had to be taken, and these were utilised as transplants. An incision was made into the upper third of the humerus, exposing the head of the bone. Its extremity for fully quarter of an inch was found to be cartilaginous. In order to refresh the bone, the cartilaginous, spike-like process was removed, leaving then a portion of bone which measured one inch and three-quarters from the tip of the acromion process. From this point a sulcus about two inches in length was made in the soft parts, in a downward direction between the muscles. The former presence of bone was nowhere indicated; there was no vestige of

FIG. 58.—INTRAHUMAN TRANSPLANTATION OF BONE. DIAPHYSIS OF RIGHT HUMERUS RESTORED BY BONE GRAFTS TAKEN FROM 6 TIBIAE.

Result 30 years after.

periosteum, and the sole guide as to the correct position into which the transplant was to be placed was an anatomical one.

Two wedges of bone were then removed from the tibia of a patient aet. 6 years, affected with anterior curves. The base of these osseous wedges consisted of the anterior portion of the tibia, along with its periosteum, the wedges gradually tapering toward the posterior portion of the tibiae. After removal, they were cut into minute fragments with the chisel, quite irrespective of the periosteum. The bulk of the fragments had no periosteum adhering to them, they having been taken from the interior of the bone.

They were then deposited into the muscular sulcus in the boy's arm and the tissues drawn over them and carefully adjusted. The wound healed without pus production. Two months after, a portion of new bone an inch in length and three-quarters of an inch in thickness was found firmly attached to the upper fragment of the humerus. In running the finger from the head of the bone toward the graft, the latter could be easily distinguished by the sudden increase in the breadth of the shaft at the point of junction of the old and new portions of bone. Now, instead of the former sharp spike-like extremity, the upper fragment ended in an obtuse terminal. Here all the grafts proliferated, grew to one another and also to the extremity of the proximal portion.

Two other wedges of bone of larger size than the first were similarly dealt with and inserted two months subsequently to the first graft, and a third couple were placed in position five months after the first. These, all fused together and to the condyles of the humerus, filled the gap in the arm to the extent of four and a

quarter inches, the humerus then measured six inches in length. Soon the utility of the arm was greatly restored (Fig. 57).

This boy, from having been in the wards for a considerable period, began to assume "airs" towards some of the boys of his own age in the ward, and one of those seized an opportunity of "setting things right," whereby the first was thrown and had his restored arm fractured between the junction of the second and third transplants. This necessitated the exposure of the bone, the two fractured extremities of which were refreshed, sutured and fixed. The two extremities of the transplanted shaft united just as a fractured normal bone would. Since this time he has been kept somewhat under observation, the patient making occasional visits to report.

Seven years after dismissal from the hospital, the humeral shaft was found to have increased in length by one and three-quarter inches, being now seven and three-quarters, and it had increased in circumference to a marked extent and had assumed a somewhat irregular shape. The length of the sound arm had, however, considerably outstripped the length of the transplanted humerus. The patient could use his grafted arm for a great many purposes—taking his food, adjusting his clothes, and in many games.

It is now thirty years since the humeral shaft was rebuilt, and during the greater part of this period the man has depended upon his physical exertions for the earning of his livelihood (Figs. 58 and 59). He worked as a joiner for many years, and now is an engineer's pattern maker. His grafted arm has increased in length, but not proportionately to the increase of the sound one. Measurements: the grafted humerus measures, in a

FIG. 59.—INTRAHUMAN TRANSPLANTATION OF BONE. THE GREATER PART OF THE SHAFT OF RIGHT HUMERUS BEING RESTORED BY BONE GRAFTS TAKEN FROM 6 TIBIAE.

straight line, from the tip of the acromion to tip of internal condyle, 10 inches, but following the curve in the bone, it is 11 inches long. The sound humerus from same points measures 14 inches—3 inches longer than the other.

Skiagraphs (Figs. 60 and 61) kindly taken by Dr. Macintyre, Glasgow, show that the increase in length of the affected arm has taken place almost entirely from the proximal epiphysis, as the new bone has been interposed between the proximal epiphysis and that portion of bone which grew from the transplantation. All but a minute portion of the distal epiphyseal cartilage was destroyed at the time of the osteomyelitis, and consequently little growth in length would be expected from this extremity.

The increase in length of the diaphysis, which has occurred from the proximal epiphyseal cartilage, may be taken as an index of the amount of growth which usually occurs from the proximal humeral epiphysis.

THE PROXIMAL HUMERAL EPIPHYSIS LEFT INTACT, THE OTHER DESTROYED.

In this human instance, however, the distal epiphyseal cartilage had been rendered in great measure functionless by disease, and the grafted portion, which at first formed the bulk of the shaft, and which at its lower end was at first contiguous with the distal epiphysis, has remained nearer that end, while the increase in length of the shaft has occurred mainly from the proximal epiphysis, and consequently the new bone has, for the most part, formed between this epiphysis and the grafts. The grafted bone, which originally measured $4\frac{1}{4}$ inches in length, and extended from the base of the humeral tuberosities to the condyles (thereby

restoring the continuity of the shaft), has been gradually pushed downwards by the new growth emanating from the proximal epiphysis, so that the grafted portion now lies toward the lower half of the shaft.

This is in accordance with the results obtained in the experimental inquiry into epiphyseal growth in the lower animal, and bears a resemblance to direct Experiment A I.

At the same time it is interesting to observe that though the distal epiphyseal cartilage was for the most part destroyed, the epiphysis itself has increased greatly in bulk, though it is probably not quite of normal size. The grafted portion of tissue, which is easily recognised from the rest of the shaft by form and contour, has increased markedly in thickness and also somewhat in length, so that there has been here interstitial osseous increase, both in the newly-formed grafted portion of the shaft and also in the distal epiphysis.

It is presumed by some that the increase in length of the diaphysis comes mainly from the epiphyseal line toward which the nutrient vessel runs. This case so far corroborates that—though the distal epiphysis was here injured, and to that extent the inferences cannot be drawn. In the present instance the length of the humerus from the tip of the acromion to the internal condyle is 10 inches, and from the same points on the sound limb the measurement is 14 inches. If the measurement be taken following the humeral curve on the grafted humerus, then the length is fully 11 inches, and perhaps this is the fairer measurement if the increase in bone has to be considered.

After the 4½ inches of bone had been added to the limb by grafting thirty years ago, the length of the humerus then measured fully 6 inches. If the measure-

FIG. 60.—SKIAGRAM. INTRAHUMAN TRANSPLANTATION OF BONE. DIAPHYSIS OF RIGHT HUMERUS RESTORED BY BONE GRAFTS TAKEN FROM 6 TIBIAE.

Result 30 years after.

ment following the curve of the bone as it is now, be taken, then the length at present is 5 inches more than formerly, namely 11 inches. The greater portion of this increase in length has come from the proximal diaphysis, still not the whole, as there has been an interstitial growth between the fragments of the transplant, as their original form has been altered, and the irregularities constituting the various parts have been separated from one another by interposition of new osseous tissue. Though there are no positive measurements to go on relatively to the increase of interstitial growth in length of the part which had been grafted, still 1 inch would be a rough estimate of that increase,—the part that had been grafted would now measure about $5\frac{1}{4}$ inches in length instead of $4\frac{1}{4}$ as formerly. This leaves 4 inches of new growth to have been produced mainly from the proximal diaphysis. It also leaves 3 inches of shortening between the length of the sound and that of the grafted arm. Could this 3 inches have been made up were the distal epiphysis in normal condition? If so, the increase in length from the proximal epiphysis (if it were normal in this case) would only have been 1 inch less than that of the distal. So that there has been some interstitial growth in length between the transplanted portions of the shaft, and interstitial growth in breadth to a marked extent between the same fragments, and this has been quite commensurate with the normal increase in breadth of the shaft. Interstitial increase in length and in breadth has also occurred in the distal humeral epiphysis—after the destruction of the epiphyseal cartilage.

CASE—*Restoration of Transverse Ramus of One-half of the Jaw by Transplantation of Bone.*—A girl, 15 years of age, had the horizontal ramus of the lower jaw

on one side extirpated owing to a diseased condition in childhood. The remaining ramus was by subsequent contraction displaced, so that it lay with its mental extremity nearly in contact with the ascending ramus of the opposite side. The remaining portions of the jaw were atrophied from disease. The teeth of the upper jaw projected over space. Mastication was in abeyance. Saliva constantly trickled from the defect. An otherwise beautiful face was hideously deformed.

Many surgeons and dentists had been applied to in turn, in the hope that they might rectify the deformity. The former would say that they could do nothing, but would advise the dentist to be consulted, as a plate might be introduced. The dentist would look at the gap and say it was impossible for him to put in a plate until the surgeon would give the patient a something to rest the plate upon.

It was resolved to try the effect of transplantation of bone, although the difficulty of securing asepsis so near the oral cavity was evident.

The first step consisted in freeing, by an incision through the skin, the extremities of the ascending ramus of the jaw on the left side and the horizontal mandible on the right. This was difficult without opening the mucous membrane, as it was so closely adherent to the extremities of the atrophied bones. After this had been accomplished, a portion of a human rib, of size sufficient to fill the gap between the left ascending ramus and the middle line of the jaw, was removed subperiosteally, divided longitudinally into strips and inserted into the gap in the soft tissues and secured to the bones on either side so as to keep the right mandible in its proper position. The soft tissues were then closed over it and the wound was dressed, and it healed.

FIG. 61.—SKIAGRAM. INTRAHUMAN TRANSPLANTATION OF BONE. DIAPHYSIS OF RIGHT HUMERUS RESTORED BY BONE GRAFTS TAKEN FROM 6 TIBIAE.

Result 30 years after.

One small portion of the transplanted bone became loose, and projecting against the scar, was shed. The remainder lived, slowly augmented in volume until firm union between the ascending right ramus and the left mandible was secured. She could then open and shut the lower jaw and use it freely. The lips came together, the overflow of saliva from the mouth ceased. The contour and symmetry of the face was restored. Some months afterwards the dentist was able to introduce a plate which rested on the newly-formed jaw, not only aiding mastication, but enhancing the appearance. The gap in the rib left by the removal of the bone taken for transplantation filled rapidly, both divided ends contributing their quota to the result.

It is now six years since the restoration of the lower jaw, and the transplanted portion has grown thicker and an increase commensurate with the development of the face has ensued. The increase in length has occurred principally from the lower extremity of the ascending ramus, which seemed to increase in size and strength to a greater extent after the transplantation than before it. The transplantation seems to have stimulated the growth in the ascending ramus. She is now perfectly well, can use the mouth freely for mastication, she speaks well, and the now symmetrical and beautiful face bears no mark of scar, as the slight one which remains is hidden under the jaw.

A second somewhat similar case, though of less extent and presenting fewer difficulties, was likewise operated on with a good result.

On many other occasions, grafting, transplanting, and re-implanting of bone have been successfully practised by me in the human subject, in the bones of the diaphyseal extremities as well as in the flat bones of

the skull, and in cancellous bone such as the patella, the condyles of the femur, etc., in order to make good defects arising from many different causes. Details of these cases are not given here, as they are not pertinent to the present inquiry—except by the way of illustrating the success of osseous grafts without periosteum or their bearing on diaphyseal growth.

CHAPTER VI.

CONCLUDING REMARKS.

Though it involves repetition, a few of the principal deductions from the foregoing data may be here given in summary.

Diaphyseal osteoblasts are generated from the nuclei of the diaphyseal cartilage cells.

The diaphyseal cartilage is but a phase in the evolution of the bone cell. When the nuclei of the cartilage cells proliferate, the cartilaginous envelopes become less distinct and finally disappear, the space being occupied by osteoblasts. These osteoblasts once formed have the power of direct and vigorous proliferation, showing great vegetative capacity; are capable, after dissemination, of growing in the midst of the soft tissues, or of being carried by the blood stream and deposited in blood clot, where they proliferate after the matrix has been supplied with new formed blood-vessels. The bone cell has the function of surrounding itself with a calcareous zone, which it controls, under the agency of the trophic nerves. As long as the bone cell remains embryonic, it exhibits the power of proliferation; but when it reaches maturity, it assumes the fixed tissue type and becomes stationary. This period is coincident with calcareous deposition and with it the cessation of active

regeneration, though its proliferating potentiality still remains.

The continuance of the embryonal form of cell,—the osteoblast,—and its rapid proliferation, tends to increase ossific production. The longer it remains embryonal and actively regenerating, the greater is the tissue production. Any agent or condition (such as prolonged movement) which, while increasing and prolonging the proliferating power of the osteoblast, does not lower its vitality, will tend to increase the bone formation. Regeneration thus produced, even under suitable physical conditions, may assume neoplastic proportions. By a somewhat similar process, stimulated by pathological conditions, part of the neoplasm found in certain tumours may be accounted for. Interstitial growth occurs in the diaphyses of long bones, contributing slightly to increase in length and markedly to circumferential augmentation. Gaps in the shafts of young bones may be made up by a similar process provided the embryonic form of the bone cell is maintained. The vegetative capacity of the bone cell is at least as great as that of the epithelial cell. Diaphyseal bone grafts live and actively proliferate in their new surroundings. Each osseous graft proliferates from its centre, the whole fusing together into one mass. In proportion to the size of the bone graft, the smaller the graft the greater is the proliferation. The proliferation of bone is proportionately in inverse ratio to the size of the graft.

Caeteris paribus the younger the animal the greater is the proliferating power of the bone cell, and the longer will it continue to proliferate before it assumes its mature form; consequently, the greater is the ossific production. The proliferating power of the osseous

tissue of old animals is greatly reduced compared with those of animals in the evolutionary period, and the osteoblasts which are poured out from them pass quickly into their mature form, which is apt to assume an eburnated condition.

Diaphyseal tissue changes, including absorption and redeposition of calcareous matter, though most active during the developmental periods of youth, are constantly recurring throughout life.

It may be deduced from the foregoing observations and experiments that diaphyseal bone is reproduced by the proliferation of osteoblasts derived from pre-existing osseous tissue, and that its regeneration takes place independently of the periosteum. The periosteum is not essential to bone production. Osseous tissue can pass through all the phases of its life, from its embryonic to its mature form, without the influence of or contact with this tissue.

The periosteum is of great use in limiting within specific boundaries the distribution of the osteoblasts, and preventing them during their evolutionary period from being scattered into the soft tissues, where their presence would be prejudicial to the function of these parts. In the loose areolar tissue existing between the periosteum and the bone the osteoblasts find nutriment for their growth and space to generate, free from undue pressure. While not under-estimating the periosteum as a limiting and protecting membrane, of great use in physiological and pathological conditions, there are no data to indicate that it can, of itself, secrete or reproduce bone. It has no osteogenic function.

Bone, bereft of its periosteum, does not therefore die, and the mere detection of bare bone by a probe is no reason for believing that such bone is either dead or

must die. If otherwise healthy, such bone is capable, not only of living, but of performing its function and proliferating if need be.

The bone-forming power of animals of the same species varies. Not only are there marked individual differences, but there may be marked variation in the proliferating power in the same individual in the same year. For instance, the bone-forming capacity is not equal during the whole adolescent period. In some months the osseous growth is extremely active compared with others, and during the former the proliferating potentiality of the osteoblast is exuberantly vigorous, while in the latter it is relatively feeble.

Bone grows in linear direction principally from the epiphyseal cartilages. Yet when these are artificially removed, osteoblasts are poured out from the shaft at the surface of the section sufficient in amount to fill the gap and to overflow into the soft tissues until solidification of the mass takes place. Soldering of the epiphyses to the diaphysis then occurs, and linear growth is greatly retarded or arrested. In the canine species, when the greater part of the shaft in its entire circumference is artificially removed, during the growing period, fresh osseous growth issues from either end and proceeds toward the centre, until the shaft is made up. Thus the growth is reversed; instead of being centrifugal it is centripetal.

When one epiphysis is mechanically fixed so as to prevent linear increase in the direction of that epiphysis, growth of the shaft still goes on, showing itself in increased lengthening of the shaft in the opposite direction, or in increased thickness of the shaft, or in bending of the bone, such as one sees in some rachitic deformities. The relations of the joint surfaces at the

opposite extremities of the bones to that of the lesion may be thus affected.

The term "epiphyseal cartilage" has been retained in the foregoing observations, as it is the term which is generally accepted. Yet this cartilage might more appropriately be called diaphyseal, as its more active portion pertains to the diaphysis.

LIST OF OBSERVATIONS AND DIRECT EXPERIMENTS.

CAN THE PERIOSTEUM PRODUCE BONE?

Direct Experiments.

1. (K) Preservation of the periosteum and subperiosteal removal of a portion of the whole circumference of the shaft (pp. 33-37).

   Result 10 *weeks after.*—Showing no bone production from the periosteum. New bone being in process of formation emanating from either extremity of the divided diaphysis tending to fill the gap from either end, the centre as yet being free from bone.

2. (W) Preservation of the entire periosteum and the subperiosteal removal of the whole shaft and epiphyses (pp. 37-38).

   Result 6 *weeks after.*—The shaft entirely wanting. No bone reproduction from the periosteum remaining *in situ.*

3. (U) Can a partially detached periosteal flap produce bone while attached at one end to the epiphysis and encircling a muscular fasciculus at the other? (pp. 38-44).

   Result 8 *weeks after.*—No reproduction of bone from the periosteal flap, but a node formed on shaft at the part from which the periosteum was removed.

4. (Y) The same as 3, except that the flap of periosteum is left attached to the bone at one end (pp. 44-47).

   Result 7 *weeks after.*—No bone reproduction round encircled muscle.

5. (X and N) Can heterotopic transplanted periosteum produce bone? A periosteal flap $2\frac{1}{4}$ inches long was raised from the radius and placed in contact with the jugular vein in the neck (pp. 47-48).

   Result 7 *weeks after.*—The flap had disappeared except at one extremity, where there was a nodule of bone the size of a barley grain, originating from osteoblasts attached to the flap while being raised from the shaft.

REGENERATION OF BONE FROM PROLIFERATION OF OSSEOUS TISSUE.

The periosteum acts as a limiting membrane to the ossific product (pp. 49-54).

Is the production of callus inherently greater in the lower animals than in man? (pp. 54-57). Fracture in leg of Red Deer. Excessive callus in man from free movement.

Direct Experiments.

Can bone deprived for the most part of its periosteum continue to grow? (p. 61).

6. (A) Periosteum removed from the entire circumference of the shaft, the bone remaining *in situ* (pp. 61-62).

   Result 12 *weeks after.*—Shaft living and growing. Shaft at some parts $\frac{1}{32}$ of an inch less in circumference than its neighbour. In other parts it retained its normal thickness.

Duhamel's Silver-Ring Experiment (pp. 62-65).

7. (B) *New Silver-Ring Experiments.*—A circle of periosteum removed from entire circumference of the shaft of right radius and a silver ring placed upon the denuded bone (pp. 65-66).

   Result 12 *weeks after.*—Showing ring completely covered by bone.

8. (P) *Second Silver-Ring Experiment.*—Two silver rings placed on centre of nude shaft (pp. 66-69). The periosteum being removed.

Result 7 *weeks after.*—Rings quite covered with bone and invisible except by X-ray.

9. *Third Silver-Ring Experiment* (L).—The periosteum having been removed a silver ring was placed on the nude shaft, adhering closely for two-thirds of its circumference, while it bulged beyond the circumference on the remaining third (pp. 70-75).

Result 12 *weeks after.*—Bone covered that part of the silver ring which was placed closely on the nude bone and filled the elbow of the bulging part of the ring, while the outer surface of this part of the ring remained free from bone but closely covered by the connective tissue lining, which had a polished surface at that part in contact with the silver ring and no osseous tissue.

THE INHERENT REPRODUCTIVE POWER OF BONE MINUS THE PERIOSTEUM.

Direct Experiment.

10 and 11. (D and E) Bone grafting in fragments without periosteum (pp. 76-80).

Result 12 *weeks after.*—Continuity of shaft restored by irregular bone mass pressing on ulna.

12 and 13. (F and G) Transplantation *en masse* without periosteum (pp. 80-83).

Result 11 *weeks after.*—Showing complete restoration of shaft without undue enlargement. No pressure on neighbouring bone.

14 and 15. (N and M) Shavings of nude bone destitute of periosteum placed among the muscles in the line of shaft (pp. 83-94).

Result 7 *weeks after.*—Continuity of shaft restored by tumour-like mass of bone causing pressure. Absorption of neighbouring bone (the ulna).

HETEROTOPIC TRANSPLANTATION OF BONE.

16. (T) Transplantation of bone shavings minus the periosteum into an intermuscular septa on the right side of the neck (p. 93).

Result 7 *weeks after.*—Showing growth of fresh bone.

17. (T) Transplantation of bone into the peritoneal cavity (pp. 94-97).

Result 6 *weeks after.*—Showing absorption of bone and also slight regeneration of bone within peritoneal cavity.

18. Bone dust made by a medium surgical drill was found unsuited for bone reproduction (p. 94).

19. Bone growing in sponge filled with granulation tissue (pp. 98-102).

20. Bone growing inside of glass tube placed in tissues (O) (pp. 102-109).

Result 8 *to* 9 *weeks after.*—Showing new osteoblastic tissue penetrating blood clot.

21. *Second Glass-Tube Experiment.*—The earliest appearance of osteoblastic bone growth penetrating blood clot and granulation tissue (pp. 109-116).

22. Osteoblasts carried by blood stream from spiculum of bone penetrating artery. Observation of false aneurism, the wall of which had become ossified from osteoblasts deposited therein (pp. 116-127).

23. Growth of bone in muscle and soft tissues. Observation on bone growing in thigh of patient. Two portions of new osseous growth in muscle measuring about 10½ inches in length (pp. 127-137). Formation of false joint.

24. Experiment (Z) showing result of osteoblasts infiltrating and surrounding muscles and tendons (p. 137).

OSSEOUS REGENERATION IN FLAT BONES.

25. Mosaic work of bone in skull (clinical observation) (pp. 138-145).

    Result 10 *years after.*—Osseous new growth uniting all the fragments to one another and to the skull.

26. Re-implantation of skull in one piece (pp. 145-146).

    Result 5 *years after.*—Osseous union to skull.

THE OSTEOGENIC POWER OCCURRING AT THE EPIPHYSEAL CARTILAGE IN REGENERATION OF BONE.

27. (Q) Subperiosteal removal of shaft of radius from $\frac{1}{4}$ of an inch from each of the epiphyseal lines, the proximal epiphysis being damaged while the distal was left intact (p. 151).

    Result 6 *weeks after.*—Growth of bone from unimpaired epiphysis vigorous, and from damaged epiphysis weak and attenuated.

28. (X) Removal of shaft of radius with its periosteum from $\frac{1}{4}$ of an inch from each epiphyseal line, a metal cap having been placed on either cut end of the shaft (pp. 152-161).

    Result 7 *weeks after.*—Epiphyseal growth has carried the metal caps toward one another, $1\frac{1}{4}$ inches from either extremity, $2\frac{1}{2}$ inches in all, and the gap in shaft has been filled by new bone.

29. (AI) The osteogenic power of the diaphysis and the epiphysis bereft of their intermediate cartilaginous plate (pp. 162-171).

    Result 12 *weeks after.*—Marked shortening of both radius and ulna—the latter not operated on but caught in callus and prevented from elongating.

30. (AII) The growth of diaphysis after removal of both the cartilagenous epiphyseal plate and the epiphysis (pp. 171-172).

    Result 12 *weeks after.*—Marked shortening and other changes.

31. Epiphyseal growth as seen after interhuman transplantation (pp. 175-191).

Result 30 *years after.*—Showing great increase in length of shaft from proximal epiphysis and little growth from the distal injured epiphysis.

32. Transplantation of bone to fill up defect in lower jaw. A portion of rib was removed subperiosteally and inserted into the gap in the jaw. The continuity of the mandible was restored. The gap in the rib was also rapidly filled in by osteoblasts issuing from both cut ends of the rib (pp. 191-195).

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